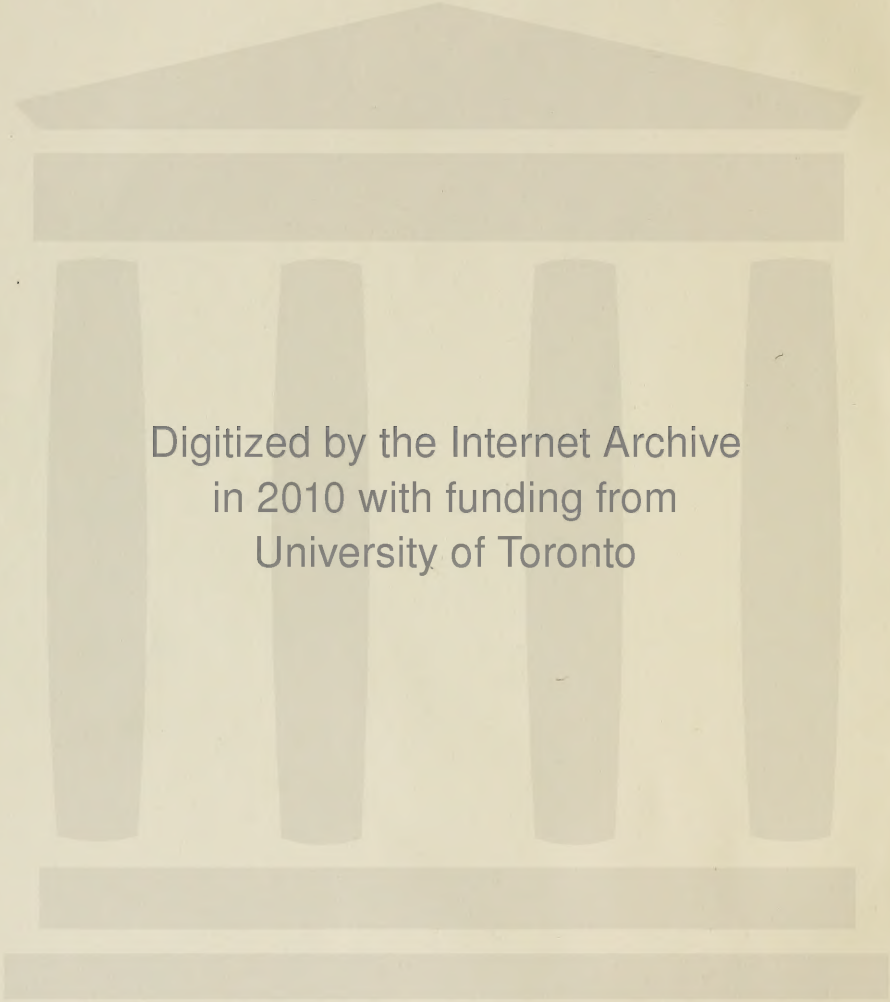
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CONTENTS.

	PAGE
Some Newer Aspects of the Pathology of Fat and Fatty Degeneration. By Henry A. Christian, M. D.,	1
Fabricius Guilhelmus Hildanus; The Father of German Surgery. By Walter B. Platt, M. D.,	7
The Importance of Testing the Ocular Muscle Balance for Near, as well as for Distant Vision. By Samuel Theobald, M. D.,	10
Infantile Paralysis of the Abdominal Muscles; with Report of a Case. By William Burgess Cornell, M. D.,	11
The Diagnostic Value of Tuberculin in Orthopedic Surgery. By W. S. Baer, M. D. and H. W. Kennard, M. D.,	13
A Practical Method of Demonstration. By W. J. Calvert, M. D.,	19
The Effect of the Bile upon the Ester-Splitting Action of Pancreatic Juice. By Albion Walter Hewlett, M. D.,	20
A Case of Right-Sided Infantile Hemiplegia, with a Description of the Pathological Changes Found in the Brain and the Spinal Cord. By Robert Reuling, M. D.,	21
Notes and News,	24
Notes on New Books,	25
Books Received,	26

SOME NEWER ASPECTS OF THE PATHOLOGY OF FAT AND FATTY DEGENERATION.[1]

By Henry A. Christian, M. D., of Boston,

Instructor in Pathology, the Medical School of Harvard University, and Second Assistant Visiting Pathologist, the Boston City Hospital.

During the past few years numerous investigators have been engaged in the study of fat in tissues. New methods of investigation have been evolved, new facts discovered, errors in previous work detected, and gradually, as a result, our ideas as to the occurrence of fat in the body, its sources, and its significance have changed. From the laboratories of the chemist, the physiologist, the pathologist, and the experimental biologist contributions to our knowledge of the subject have come. These researches are of great interest, the methods used often very ingenious, and the results of much importance in the proper interpretation of pathological findings. Consequently it has seemed to me preferable to review this afternoon some of this more recent work and to discuss its interpretation rather than to limit myself strictly to the narrow field in which I myself have worked. The subject which I have selected is then a broad one and necessarily in the time at my disposal I must confine my remarks to its more important phases and even these can be discussed in but a superficial fragmentary fashion.

[1] A lecture delivered to the post-graduate classes of the Johns Hopkins University, May 9, 1904.

I. *Methods of technique.*—At the outset it may be well to speak of the methods and criteria at our disposal for the detection of fat in tissues. These may be divided into two groups: (a) those which visually demonstrate the fat within tissue, and (b) those which separate fat from tissue.

The latter group (b) comprises various chemical methods of analysis. They involve extraction of the fat by ether or other extractives in appropriate apparatus, an estimation of the quantities obtained, and a determination of the nature of the extracted substances.

In the first group (a) properly come those physical properties of fat and fatty tissue macroscopically evident, such as the tawny yellow color, greasy feel, indistinctness of normal markings, and increased friableness of the fatty liver; and those microscopically evident as the high refraction of the fat droplets and its solubility relations. These criteria, however, do not suffice; for small amounts of fat are not macroscopically evident; conditions of simple anæmia may be misinterpreted as fat; microscopically error may arise from the high refraction of substances not fat, while in unstained tissue little knowledge can be had of the relation of fat drop to cell struc-

ture. Hence arises the necessity for staining methods, and these form the most important part of the first group.

Of staining methods there are two kinds, one giving a negative, the other a positive picture. In the first are all methods which preserve and stain the cytoplasm and nucleus while the fat is dissolved out, leaving a vacuole in its place. Such preparations give evidence of the relation of the fat droplet to cell structure, provided the fat droplet is larger than a certain minimal size, but they require other proof of the fatty nature of the substance from whose former presence the vacuole has resulted.

This proof is given in the use of certain stains which may be applied directly to the fresh tissue or to it after formaldehyde fixation. These stains are osmium tetraoxide (osmic acid), Sudan III, Scharlach R, and Indophenol.

Of these stains osmium tetraoxide has been longest in use and is the method still most generally used for the detection of fat. It is reduced, probably to metallic osmium, by the fat and the fat droplet appears of a dark brown to black color. It can be employed in a variety of well known combinations. The chief advantage of its use is the fact that fat after treatment with it becomes insoluble in the fluids necessary for embedding in celloidin and paraffin. Its disadvantages are its imperfect penetration into blocks of tissue, the fact that it stains other substances than fat, and does not stain all forms of fat. The latter is very important and was first emphasized in 1894 by Altmann who showed that osmium tetraoxide stained only olein and oleic acid and was to be regarded solely as a reagent for the demonstration of these components of fat. That osmium does not stain all forms of fat has been proven by a number of investigations since then, though there has been some discussion concerning the chemical nature of the fat to which its action is limited. As a single example of this limitation in the use of osmium tetraoxide, I found in the cells in the early stages of pneumonic exudations much fat present in small droplets which failed to stain by the osmium method either directly or after secondary reduction in alcohol but stained characteristically with Scharlach R and Sudan III. Further I showed that this was not due to the physical condition of fineness of emulsion, but to some peculiarity in the chemical composition of the fat in question.

For the above reasons the general use of osmium tetraoxide in the past has led undoubtedly to error in our estimates of fatty changes, and after its use alone conclusions as to the presence or absence of fat in a tissue should not be drawn. Yet used in conjunction with other methods it is of much value in the study of pathological processes.

Sudan III and Scharlach R, the former introduced into microscopic technique by Daddi (1896), the latter by Michaelis (1901), stain fat red. They can be used either on fresh tissue or after formaldehyde fixation. Tissue so stained can be mounted in glycerine. These compounds stain, so far as our present knowledge goes, all three forms of fat and only substances of a fatty nature. Of the two Scharlach R is preferable because it stains fat more intensely, tints the other tissues less, and is less likely to precipitate in tissue than Sudan III. It is best used in a saturated solution in 70% alcohol in which the sections are stained 24 hours to 48 hours or in a saturated alkaline alcoholic solution for a shorter time, a method recommended by Herxheimer. Of the two methods I personally prefer the former.

Sudan III and Scharlach R seem to be the best fat stains at our service. The disadvantage of them is the necessity of application to frozen sections and mounting in glycerine. These stains merely demonstrate the presence in tissue of certain fatty substances without indicating their chemical nature. The presence of these substances in tissue indicates certain metabolic activities of the cells to be discussed later.

Indophenol stains fat blue. It seems not to have been extensively used, and I have had no experience with it.

II. *Adipose tissue.*—In the body, fat is found in certain regions in the form of adipose tissue. In addition it is present in many of the organs and tissues under normal conditions. The chief sites of adipose tissue are in the subcutaneous tissues, in the omentum and mesentery, retroperitoneally, especially about the kidney, and to a less extent beneath the pericardium and parietal pleura. In these situations the fat is often present in very large amount and these sites form in the body the normal storehouses for fat and represent the true fat organs.

Here the fat cells are closely packed to form lobules of irregular shape and varying size. Between the lobules there is a moderate amount of connective tissue in which course the larger blood vessels and lymphatics. Between the individual cells the connective tissue framework is reduced to a minimum. With the anilin blue connective tissue stain only here and there fine fibrils appear, while with the phosphotungstic acid hæmatein stain a few scattered fibroglia fibrils can be made out, generally in association with connective tissue cells lying in close apposition to a capillary blood vessel. Elastic tissue occurs only in association with the larger blood vessels. It is thus evident that the cells of adipose tissue, of mesenchymal origin, have almost entirely lost their power of forming fibrillar intercellular substance. Instead they seem only concerned in fat metabolism and in this sense are specialized in function.

The most striking feature of adipose tissue is its great vascularity. This is especially evident where for any reason the fat is congested. Then between almost every cell can be seen a thin walled capillary—a surprising richness in vessels if our ideas have been based on the ordinary uninjected specimen of fat. This very intimate relation between blood capillary and fat cell must be very important in the metabolic functions played by the fat tissue. The adipose tissue is not, I think, to be regarded as merely a passive storehouse for fat but rather as a diffuse fat vascular organ in which great activity of fat synthesis or fat analysis may take place.

Fat cells vary somewhat in appearance though in the adipose tissue of the adult the common form is a large cell containing a single large fat droplet. The cytoplasm is reduced to a thin rim or membrane which takes a violet tint

in specimens stained by the anilin blue connective tissue method. This rim is almost homogeneous in appearance. The nucleus is crowded to one side and flattened out to accommodate itself to the curvature of the fat droplet. About it is a small amount of granular cytoplasm which often contains bright yellow granular pigment. Within the nucleus there is present almost always a single or several fat droplets, crowding aside the nucleoplasm and chromatin of an otherwise vesicular nucleus. These fat droplets are usually small (1 to 2 micra) but often are larger, may exceed in diameter the thickness of the nucleus and present as a distinct boss on one or both surfaces. In nuclei at times they are so numerous that the nuclear substance is present merely as a delicate reticulum enmeshing the fat droplets. Their very common occurrence in the nuclei of fat cells and the absence of any evidence of injurious action on the chromatin makes it very certain that they are not to be regarded as a degenerative phenomenon of the nuclei. Their presence often aids in distinguishing the nucleus of the fat cells from those of the scattered connective tissue corpuscles between them, for I never have found fat vacuoles in the nucleus of a cell distinctly between the fat cells and of connective tissue character or in the endothelial cells of blood vessels.

The cell described above is by far the most frequent in adipose tissue and in lipomata, but another type occurs. This is a cell slightly smaller, containing not a single fat droplet, but several, often many. In these there is proportionately more granular cytoplasm and the nucleus is not so crowded to the periphery though generally occupying the outer part of the cell. Sometimes the nucleus is in the center. Such cells occur singly, but much more often in groups of three or four to a dozen or more and were found more often in the fat of the omentum and the perinephric region than in subcutaneous adipose tissue. They resemble closely the fat cells occurring in the "brown fat" of the rat and other mammals, in the mesenteric fat of a fœtus at term which I have recently examined, and in a peculiar lipoma of the neck excised at the Boston City Hospital. Their exact significance cannot be stated, but as in some cases transitions to the first or common type can be made out, it seems probable that they are cells showing very active fat metabolism, and more probably fat synthesis than fat splitting.

Not infrequently in fat tissue or about small groups of fat cells occurs a third type, smaller than either of the two preceding types of cell and filled with very many small fat droplets. The nucleus of this cell is vesicular, centrally situated and has never been seen to be vacuolated. Such cells are numerous in adipose tissue undergoing repair, such as healing abdominal wounds. Here they occur singly or in groups about fat droplets. Sometimes they are larger and multinucleated. They also occur about the fat cells of the bone marrow in certain infectious diseases, as small-pox. Scattered groups of them I have seen in one specimen of lipoma and numerous cells of similar appearance were found in a specimen of breast in an inflammatory focus, associated with tissue destruction and the escape of colostrum. From the size, structure, and occurrence of these cells they seem to be of endothelial character and are probably concerned in the removal of fat set free in the tissues by injury of the fat cells —are phagocytic. This explanation seems more in accord with their occurrence than that they are young fat cells concerned in the regeneration of adipose tissue.

III. *Fat in organs and tissues under normal conditions.*— Before considering the fat normally present in the body other than in adipose tissue, it is necessary to emphasize the necessity of distinguishing between fat that can be visually demonstrated in a tissue and fat that can be extracted from that same tissue. A single example is sufficient to make this difference clear. In the normal human kidney almost no fat can be demonstrated in the cells by any of our staining methods; yet by the method of extraction the kidney is shown to contain under normal conditions a very considerable amount of fat, according to Rosenfeld, from 16 to 23%. In a diseased condition on the other hand, the kidney cells under the microscope may show a rich supply of fat droplets, an evident difference as shown by the microscope from the normal kidney. However, from that same kidney, chemical analysis may yield no more fat than from a normal kidney. There is then an evident difference between the results given in the two methods and the presence or absence of fat as determined by one method or the other, obviously has a different significance. Consequently the method used in a given case must be stated in order to avoid confusion in interpretation of results.

Fat capable of visual demonstration is known, however, to occur very much more generally in the body tissues than was formerly held. This knowledge has come mainly since the introduction of the stains, Sudan III and Scharlach R and is the result of work of Sata, Stangl, Fischer, Herxheimer, Hansemann, Cordes, Erdheim, and others. They have shown that fat is present in almost all of the glands of the body and occurs there under normal conditions in some way associated with cell metabolism.

The almost constant presence of fat in the liver has been long recognized and its large amount distinguishes it from other organs, so that the liver is very generally regarded as a fat depot analogous to the adipose tissue. Perhaps here the fat may undergo some change preparatory to its utilization by the other cells and so stand in a different relation to liver cells. That fat is normally present in the epithelium of the salivary glands, pancreas, adrenal, testis, ovary, thyroid, thymus, sweat and sebaceous glands, and breast is not so generally recognized. Of particular interest to the pathologist is the question of the occurrence of fat in the kidney and heart.

In the kidney of many of the lower animals fat occurs under normal conditions, particularly in the straight tubules where it has a basal position in the cell. In the human kidney it seems that small amounts of fat may be normally present and that slight amounts of fat cannot without other evidence be considered as pathological. However, any considerable increase of fat may be regarded as pathological.

Practically the same holds true of the heart muscle where Ostertag has found fat in normal guinea pigs and pigeons

and Fibiger in normal cats. Lubarsch has shown that fat is associated with the perinuclear pigment of the heart muscle as it is with the intracellular pigment of nerve cells. Consequently in these two most important organs, the heart and the kidney, it is not the finding of small amounts of fat which can be interpreted as indicative of pathological change, but the occurrence of more than a certain minimal amount of visually demonstrable fat, at the same time remembering that fat can be chemically extracted from both organs under normal conditions in considerable amount. Of the other tissues, skeletal muscles, endothelium of blood vessels, connective tissue corpuscles, and leucocytes generally contain fat. Herxheimer, reviewing the question, finds of all the tissues, the spleen and lymph nodes are almost the sole ones that are normally fat free.

In most organs where fat occurs it is very scant in fœtal life if present at all but gradually increases in amount after birth. Such fat can be regarded in no other light than the result of the metabolic activity of the cells and bears no relation to cell degeneration.

IV. *Fat in tissues under abnormal conditions.*—Of far greater interest is the occurrence of fat in tissues under abnormal conditions. Many studies have been made of this subject and the meaning of the findings has been the subject of much discussion. The frequency with which considerable amounts of stainable fat is found in the liver, heart, and kidney at autopsy is generally known, but other organs have not been so systematically studied. For several years at the Boston City Hospital we have made systematic examinations of the heart, liver, and kidney, at first by means of teased specimens or frozen sections treated with acetic acid, during the past year or so by means of the Sudan III and Scharlach R technique. This has impressed us with the great frequency of the finding of fat in autopsy tissues.

In our last 50 autopsies the heart, liver, kidney, and spleen have been studied by the Scharlach R method. These 50 cases may be roughly classified as follows: In 25 the immediate cause of death was some acute disease such as pneumonia, peritonitis, or diphtheria; 17 showed chronic processes; 8 were chronic processes with a definite superimposed acute infection. Only four bodies were emaciated, and even here there was considerable remaining subcutaneous fat. The hearts of these cases showed fat within the muscle fibres of the left ventricle in 56 per cent of the cases; in 28 per cent in slight amount, in 20 per cent in considerable amount, and in 10 per cent in very large amount. Of the kidneys 74 per cent showed fat, 38 per cent in slight amount, 30 per cent in moderate amount, and 6 per cent in large amount. Of livers only two were fat free, while 40 per cent showed a slight amount, 50 per cent a considerable amount, and 4 per cent a very large amount of fat. In 39 of these autopsies the spleen was studied; 18 were fat free, 21 contained small amounts of fat. In none of these cases were all of the viscera fat free, but in several fat was present only in the liver.

In the heart the fat was found in most cases not throughout the tissue, but in groups of fibres. Likewise in the kidney the localization was almost always a focal one and where the fat was very slight in amount it occurred most frequently in the basal end of the epithelial cells of the loops of Henle or of the collecting tubules. In the spleen the fat was found as a rule either in the capsule and trabeculæ, or in the endothelium of the blood vessels. Only in five cases was it elsewhere, once in the pulp cells, and four times in proliferated endothelial cells in the centers of Malpighian bodies. These last four were cases of diphtheria.

In the heart, kidney, and spleen the fat was practically always in the form of fine droplets, in the liver it was commonly in large droplets or as a mixture of small and large. In only eight cases were fine droplets alone present in the liver. Two of these were chronic, the other six acute cases, pneumonia or diphtheria.

The fat then has been associated with a very great variety of processes now chronic, now acute. What has been most striking is the great variety in distribution in the various organs in a given case and in different parts of the same organ or tissue.

In 28 consecutive autopsies I have studied the fat in the myocardium, pectoralis major, and psoas major muscles. Portions were taken from the papillary muscle and intraventricular septum of the heart and from two parts of the above mentioned skeletal muscles. These examinations showed that not infrequently the myocardium exhibited marked fatty change while the skeletal muscles were little affected or the converse. Sometimes there was a considerable difference between the two skeletal muscles. The figures were:

	Fat absent.	Fat present slight amount.	Fat present moderate amount.	Fat present large amount.
Heart	5	10	4	9
Pectoralis major	5	9	6	8
Psoas major	8	6	7	7

As a result of these and other studies there has been a growing feeling of a very imperfect knowledge of the causes underlying the distribution of the fat in a given case and the meaning of its presence. That this feeling is a very general one is evidenced by the present active discussion as to the sources and significance of intracellular fat.

Under the influence of a variety of conditions, such as general or local anæmia, venous stasis, phosphorus, arsenic, and lead poisoning, acute infectious diseases, many bacterial infections, fat appears in cells in increased amount. To the fat various origins could be assigned. This fat might be formed within the cell either from proteid or from other constituent of the cell. It might come from without the cell being transported thither by the lymph or blood stream.

In 1847 Virchow taught that the fat of fatty degeneration was formed within the cell as a result of the destruction of cell proteid. This dictum was accepted by pathologists until very recently and is yet the explanation very generally given in text books on pathology. What evidence is there for such an assumption?

Voit and Pettenkofer as a result of their work in 1862-71 claimed that the body fat was formed from ingested pro-

teid. Voit had fed dogs on lean meat and in excreta regained all the nitrogen of fed muscle proteid, but not all of the carbon. Of the carbon a greater part remained in the body, more than could have been converted into glycogen, and so he assumed that it was stored as fat. This was accepted until Pflüger in 1891 vigorously attacked these views. He showed that Voit and his pupils had based their calculations on an erroneous assumption of the carbon and nitrogen content of the lean meat, and that by using the correct figures the retained carbon disappeared, and with it the bases of Voit's assumption of the formation of body fat from food proteids. Since then numerous metabolism investigations have been made, the results of most of which negative the assumption of Voit, so at the present day it seems proven that body fat is not formed from the ingested proteid, but from food carbohydrates and food fat. Voit had further claimed in support of his view a formation of fat from proteid in adipocere, the ripening of cheese, and the secretion of milk. Later work has shown the first two to be due to bacterial activity, while the fat of milk is known to come from the body fat. So in physiology there is no evidence of a formation of fat from proteid in the sense of Virchow, other than the result of vegetable life, a condition which evidently does not enter into the present consideration.

One by one the various pathological conditions regarded as typical examples of fatty degeneration have been submitted to the most careful microscopic and chemical scrutiny or subjected to the proof of animal experimentation.

In cases of phosphorus poisoning the cells of the liver and other viscera become filled with fat droplets. It was long held that this fat was formed from the proteid of the liver cell. In 1883 Lebedeff combated this and claimed that the fat came from the fat depots and did not arise within the cell itself. He based his claims on finding linseed oil after phosphorus poisoning in the liver of fasting dogs which he had previously fed on linseed oil. Rosenfeld by a series of careful experiments, the first reported in 1897, demonstrated the transportation of fat in phosphorus poisoning. He starved dogs until their body fat was reduced to a minimum. He then fed them on lean meat and mutton fat until their fat depots were filled with mutton fat. Again these dogs were starved until no fat was in the liver, that disappearing very much earlier than the fat of the fat depots. The administration of phosphorus now brought about a marked appearance of fat in the liver. Analysis showed this fat in the liver to have the composition of mutton fat which points to a transportation of fat from the fat depots, not a formation from the proteid of the liver cells, in which case the fat would have had the composition of that normal for the dog. Further in starved dogs, whose body fats have been used up, phosphorus poisoning produced no fatty degeneration because there was no fat for transport. Fibiger obtained the same results in chickens after phosphorus poisoning and in rabbits after diphtheria toxin. As early as 1864 Leisering had noted his failure to get fat in the liver after giving phosphorus to two lean chickens. Clinically this is supported by the absence of fatty liver after phosphorus poisoning in a very lean patient reported by Lebedeff from Kussmaul's clinic. That the fat comes from the body fat by the way of the circulation is supported by finding the fat increased in the blood in cases of phosphorus poisoning, observations of Méhu, Rosenfeld, and Daddi. Various objections raised to the experiments of Rosenfeld have been one after another successfully met, and his results confirmed by others. Analysis of these livers shows, besides changes in the fat, a disappearance of glycogen (Saikowski, Luchsinger, Stolnikow, and others) and the formation of split products of proteids. The latter indicate cell degeneration, but too little to account for the fat—the two processes fatty infiltration and cell degeneration go hand in hand. Very similar results have been obtained after the action of other poisons as arsenic, chloroform, and phloridzin. Leick and Winkler, using this method of Rosenfeld, have shown that the fat in the heart after phosphorus poisoning originates from body fat by transport.

Athanasiu and Taylor attacked the problem in another way. They used frogs. Taylor in his experiments took a dozen frogs and divided them into two groups, each of which had the same number of frogs and the same total weight. To one group he gave phosphorus, the other remained as controls. When a phosphorus frog died a control frog of equal size was killed. The bodies of all were dried, pulverized, and their fat extracted. The phosphorus frogs had fatty livers but their total fat was not increased which is evidence of a redistribution of fat—not a new formation.

There is also much morphological evidence of fat transportation. Fat is often seen deposited in that part of the cell adjacent to a blood capillary. This has been noted in the adrenal, is not infrequent in the liver, while in the kidney the basal end of the cell is the common locus of the fat. In renal infarcts it is the boundary zone, where circulation or fluid transfusion is maintained about injured cells, that accumulates fat, while the center of the infarct and the uninjured parts of the kidney remain fat free. Fischler in his studies of this condition concludes that the appearance of the fat depends on the circulation; there is no fat deposited where there is no circulation, and further, it depends on the cells themselves; injured cells take up fat, but they must be living, not dead cells. Fat comes in a soluble form and the cells must be possessed of metabolic activity in order to synthesize this material into demonstrable fat droplets. The same relation of fat deposition holds for tuberculous caseous areas, about which there is a boundary zone of fat. Hagemeister in a study of granulation tissue, tuberculosis, kidney infarcts, etc., places more stress on the relations between fat appearance and circulatory disturbances, and even minimizes the part played by the cells themselves. He thinks fat disappears where there is an increased flow of blood and lymph, but is taken up by cells where there is an obstructed flow. Arnold as a result of numerous experiments in which he injected fats, soaps, etc., emphasizes strongly the transport of fat in so-called fatty degeneration.

Fischler in experiments on isolated kidneys showed the synthesis and deposition of fat in the tubular epithelium from soaps circulated through the organ. In my studies of pneumonia I found the same fat within the polynuclear cells of the circulating blood which I found within the cells of the early exudates and believed that the leucocytes arrived in the exudate already containing the fat.

As a result of all of these observations, it seems that, in a variety of conditions, formerly regarded as true fatty degeneration (that is, a formation of fat from proteid), the fat arises from without the cell, is transported thither. Does all of the fat so arise? This is very much more difficult to prove, but seems to be answered for the liver under certain conditions by the following work of Rosenfeld. Dogs with fat depots stored with mutton fat were prepared as above and then starved to remove the fat from their livers. A part of the liver was then excised, the amount of fat determined and its iodin number found. The animals now received phloridzin or ol. pulegii, after which their liver fat and body fat were similarly analyzed. The results are shown in the following table:

	Leber.					
	Exstirpiertes Stück.		Uebrige Leber			Depotfett
	Fett %	Jodzahl	Fett %	Jodzahl gefunden	Jodzahl berechnet	Jodzahl
A. Phloridzin...	16.7	106.5	30.0	78.8	81.4	49–52
B. Ol. Pulegii...	14.03	71.3	19.8	61.2	66.2	53.8
C. Ol. Pulegii...	22.5	67.8	33.33	60.8	62.2	50.4

An examination of this shows a close agreement between the calculated iodin number of the liver fat and that actually found after treatment—a very satisfactory proof of the origin of all the fat of the liver from the fat depots under these conditions.

Against the assumption, that all fat is transported to the cell, are the careful analyses of abnormal kidneys in which Rosenfeld found no considerable increase of extractive fat though microscopically there was the condition of fatty degeneration. Similar results have been found for areas of cerebral softening. In tissue preserved aseptically without the body according to many observers fat droplets appear (autolysis). Here there is no circulation. Consequently it seems that we must assume a formation of fat within the cells. There is no evidence of a formation of fat from proteid though the possibility cannot be denied. Fatty bodies do occur in organs where we cannot detect them microscopically. They may be in a state of such extremely fine division as to escape detection—a change of physical condition would give their appearance as fine droplets. They may be in a loose combination with proteid or other substance—a combined fat not visually demonstrable which under certain conditions splits into free fat and some other body. Taylor has furnished some evidence of this. We may have compounds such as protagon or lecithin in whose complicated molecules fatty radicals exist to be later split off. In some such form it seems fat-like or fat-related bodies exist in protoplasm and at present we are not justified in deriving all fat that appears pathologically from sources without the cell.

Of fatty degeneration in the sense of Virchow we have no proof. At present our knowledge is in too unsettled a condition to be justified in the creation of new terms. We must wait until chemical and experimental study can give us more data before we can create new names which will perfectly harmonize with the facts of the case. For the present it seems best to continue the use of the old terms—fatty infiltration and fatty degeneration, and define the latter as the appearance of fat in cells which have undergone some form of injury. This fat arises from without and is transported to the cell or arises within the cell from fat-related substances. The former probably explains the greater part of the fat, though in this respect tissues may vary. At present there is most evidence for a purely extracellular origin of fat in the liver, very much less for the kidney. Conditions determining the one and the other need further study.

Here I must leave the subject. I realize how imperfectly the ground has been covered, but I trust the following points have been sufficiently emphasized:

(1) That osmic acid does not stain all forms of fat and fat alone, and so is but an imperfect method of demonstrating fat. Sudan III and Scharlach R, though having disadvantages, give more satisfactory results. (2) That visually demonstrable fat is present normally in very many cells of the body while extractive fat occurs in practically all of the tissues. (3) That under abnormal conditions visually demonstrable fat appears in cells in increased amount and is an index of cell injury. (4) That fatty infiltration is the physiological appearance of fat in normal cells and fatty degeneration is the appearance of fat in injured cells; the fat is an index rather than the direct result of the cell degeneration. (5) That in both, the origin of the fat is probably the same and mainly from without the cell by transport from fat depots elsewhere, but may arise within the cell from fat-related bodies, not from proteid.

STUDIES IN TYPHOID FEVER.

SERIES I-II-III.

The papers on Typhoid Fever, edited by Professor William Osler, M. D., and printed in Volumes IV, V and VIII of the Johns Hopkins Hospital Reports, have been brought together and bound in cloth.

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The price is $5.00 per copy. Address The Johns Hopkins Press, Baltimore, Maryland.

FABRICIUS GUILHELMUS HILDANUS: THE FATHER OF GERMAN SURGERY.[1]

By Walter B. Platt, M. D.

The father of German surgery, or as he has been called the Ambroise Paré of Germany, was born on June 25, 1560 in Hilden, Germany, not far from Düsseldorf, as plain Wilhelm Fabry. Early in his professional career he latinized his name after the fashion of the day, making it Fabricius Guilhelmus Hildanus, now often called simply Hildanus, to distinguished him from another Fabricius. As Latin was the international tongue of letters, religion, and what there was then of science in Europe, this was not as absurd and pedantic as it now seems. The fraternity of letters was far less national than at present, and students and scholars went from land to land seeking the knowledge they could not otherwise obtain. For these reasons most of the important works of Hildanus were written in Latin.

His father was clerk of one of the courts, a man of parts we hear, and at least respectable and respected. Hildanus himself speaks of his father as "homo literatus."

The father dying when Hildanus was but a year old he was left to the care of his mother who speedily remarried. Of our surgeon's boyhood we know little except that he seemed to have unusual vitality, vastly enjoyed swimming, and suffered a paralysis of the tongue at the age of twelve in consequence of swimming too long in cold water. It was many years before he perfectly recovered his speech. Left with little or no means early in life the good poet Utenhof assisted him, sent him to school in Cologne, and as he grew older urged him to become a physician. Medicine was not at all to his taste and from the first he preferred surgery. In 1576 when but 15 years of age he entered the service of a surgeon named Dumgens at Neuss, with whom he remained four years, after which he joined himself to the surgeon of the Duke of Cleve. Now began a series of wanderings from place to place.

Going to Metz in 1585 he went thence to Geneva where he operated on a strangulated hernia. Two years later he married Marie Colinet, who turned out to be a helpmeet indeed. Leaving Switzerland in 1588 he returned to Hilden for 3 years, going thence to Cologne where he practiced from 1591 to 1596.

Besides practicing surgery arduously, he cultivated the science of medicine in its broadest sense, and wrote many monographs and descriptions of surgical procedures. In 1593 he published what is perhaps the best known of his writings at the present time, "De Gangrena et Sphacelo." He also described the most important of the valvular folds of mucous membrane of the rectum, and demonstrated its function.

We find him again at Lausanne in Switzerland in 1596 where he worked hard at his anatomy and made many autopsies, but he could not remain very long in one place and went back to Cologne in 1597 where he remained 3 years. He was in Lausanne again in 1600, whence he fared to Payern. In 1607 he published a work on dysentery, and constructed a model of an eye for the use of students.

His family had the bubonic plague in 1613 and most of his children died of it. After he thought he was at last rid of it, the plague reappeared in his house after an intermission of months.

About this time von Hildanus became a great sufferer with a neuralgia or gouty headache, which he finally traced to a particular kind of wine of which he was very fond. He also was a martyr to gout.

Those who are afflicted in a similar way may console themselves with the thought that they are in good company for numbers of our greatest (as well as our laziest) men have had the gout. Hildanus now lived in Berne for a season. In 1619 he finished "Observationum et Curationum Chirurgicarum Centuriæ IV," and wrote his hundred letters to his friends.

He wrote "Observationum et Curationum Chirurgicarum Centuriæ VI," his last, in 1623, and in 1620 on a "Christian way to Eat." In 1624 he wrote upon the value of anatomy.

In 1626 he wrote his well-known work on Stone, and two years later was very ill with the gout.

After this it is quite natural, that he should write upon the "Preservation of the Health" by the use of certain warm springs.

We think we can see the steady progress of gouty nephritis as in 1631 he had bronchitis, and was often annoyed by asthma.

He died on February 14, 1634, aet. 74 years.

Of all his children, but one, a son, survived his father.

Hildanus was a deeply religious man, a very conscientious operator, not at all vain; on the contrary he was always dissatisfied with his work, while the amount he accomplished was prodigious. He always declined to operate when he thought the outlook a fatal one. His letters were very numerous. He is said to have corresponded with 150 physicians and other learned men. Although very modest he did well financially, unlike most men of his type. He always showed great mental activity.

Hildanus.

In the time of Hildanus, Wesling writes from Venice comparing German surgery with that of Venice, saying "Surgery has a somewhat better status here, although even here there are those called surgeons who come from the dregs of the population, so that if Venice had to take the field, about 2000 dirty barbers and enema givers would enlist as surgeons."

[1] Read before the Johns Hopkins Hospital Historical Club, March 14, 1904.

Hildanus gives a few examples of the state of surgery in his time as follows:

"A cabinet maker who was watching the drilling of an artillery battery, was wounded in the breast by the discharge of a blank charge from standing too near, in consequence of which the covering of the chest was torn away down to the ribs. A barber surgeon who was summoned, seeing a bare rib, seized it with a pair of forceps, and tried with all his force to drag it away, thinking it some part of the ramrod. Fortunately a bystander drove the barber away, applied a suitable dressing to the exposed ribs, and in time the man recovered."

Hildanus says "In spite of all their ignorance, the surgeons thought they knew better than educated physicians" and he relates how in one case where he "had refused to amputate the limb of a man who had senile gangrene, a barber did the operation, amputating the thigh which of course speedily became gangrenous at the seat of operation, whereupon the patient died;" Hildanus writes further: "Christian pity often makes me weep over the doings of those men who play so recklessly with human life." (Archiv f. klin. Chirurgie, 1865, vi, by Meyer Ahrens.)

Although a surgeon, Hildanus knew his anatomy better than most professors of that branch, and laid great stress upon a thorough knowledge of this subject. He called anatomy the "key" to every department of medicine, and the "rudder" to all medical practice.

He demanded that priests should have some knowledge of it, and that lawyers should likewise have an acquaintance with anatomy that they might apply torture with more effect and discretion to criminals, so as to avoid sudden death, or a confession of crimes which had not been committed. He saw the importance of some education of midwives in anatomy that they might know enough to call in a physician before it was too late to do any good.

At the end of the 16th and beginning of the 17th century it was difficult to obtain bodies to dissect in Switzerland. In the year 1601 when he demonstrated the valvulæ Bauhini (of the rectum) on a cadaver, it is related that he carefully preserved the fat of the subject to send to a French physician who wished to use it as a therapeutic agent.

Hildanus' first good anatomical preparation was a maceration, showing the blood-vessels of the abdominal viscera, notably those of the liver, kidneys and genito-urinary system.

According to the custom of his time, he finds all manner of curious analogies between the human body, and the universe in general.

He makes gruesome remarks upon the advisability of so applying torture to criminals as not to fracture the scapulæ by bending back the arms too far, something he has often seen, since men thus treated would be apt to confess to crimes they had never committed.

Like a true scientific surgeon he attached great importance to a knowledge of pathological anatomy. He took an especial interest in congenital malformations, making a number of drawings in these weird creations. He made moreover a collection of bones showing the healing of fractures, and in a letter to Prof. Paw he eulogized the value of Comparative Anatomy, Botany and Chemistry.

Like most physicians of his time he was a believer in the medicinal virtues of various disgusting agents, such as portions of vipers, and of dried toads. Mineral water baths were objects of his admiration as healing agents, and he wrote a monograph in 1629 on the preservation of health by the use of certain thermal springs. He wrote much about the plague or what he thought was the plague, which destroyed so many human lives and spoke of the inefficacy of any known treatment, although he felt sure that those who had issues in their arms did not die of it.

Hildanus was a great believer in the use of minute varieties of instruments, and spent much time and ingenuity in devising them. One of these was a bullet extractor, consisting of a tube which was introduced down the track of the bullet until it reached the ball when a cork-screw-like device was protruded. This was supposed to enter the ball, so as to allow of its removal by traction. He treated the bites of rabid animals with all sorts of irritating mixtures, but also with the actual cautery.

He combated the idea advanced at that time, that in cranial fracture the depressed bone should not be elevated, and invented a somewhat impracticable instrument to raise the depressed fragments. He makes frequent use of egg albumen as a styptic, discusses polypi, and describes the operation for the removal of the breast for cancer. As far as the anatomical part of it is concerned he operated much as we did 20 years ago. The use of caustics in these cases which had a charm for many patients and physicians, he deplored.

Concerning the radical cure of inguinal hernia, he remarks the extreme rarity of such cures in his time, but details one in a well-known personage where such a result was achieved by several months rest in bed in a horizontal position and the continual use of a truss.

It is interesting to note that Hildanus was a firm believer in the virtues of issues, and fontanelles, devices to secure suppuration, as a means of warding off disease by providing an outlet for "vicious humours" which were supposed to be their cause.

He invented a suspensory bandage, and urinals to be worn by the patient when going about, and also club-foot apparatus. Fabricius was aided by a help-meet indeed, who was skillful in the art of obstetrics, for his wife was often present in difficult cases.

At the beginning of the 17th century no one thought of calling in a physician until midwives had utterly failed. It was then usually too late to do much for the patient, for these midwives were a wretchedly ignorant lot. In a Treatise on Lithotomy published in Basel 1629, Hildanus warns all ignorant persons not to undertake to cut for stone, and in the course of his discussion of the operation he says, "The patient should prepare himself in all ways for death before the operation, he should make his will and ask for prayers in church." That Hildanus had an exalted ideal of a surgeon will be seen when we learn that "he should before all, fear God, be

true, pious, upright, not given to cursing or swearing, he should not be addicted to drinking, whores or gambling." "The patient should avoid all physicians who gossip or chatter much, or who boast of their powers as if none were equal to them."

Furthermore he says "a surgeon should not be merely an empiric guided alone by his experience, but should have studied more in the science and groundwork of his profession."

Hildanus operated for stone in the male bladder usually by a lateral incision in the perineum, but they were sometimes removed through the rectum, while in women he removed them either by way of the vagina or urethra. When patients came to the surgeon with very large stones, Fabricius advised that operation be declined, and that they be turned over to their spiritual advisers.

Stones in the bladder at this time were often removed in several sittings, the incision being the first sitting, when unless the stone presented at the opening, delay was advised until it did, when an attempt was made at extraction. If this did not succeed, another wait was advised, the patient being put through a course of medical treatment tending to relax the opening and eject the stone.

Meyer Ahrens mentions a "stone-cutter" of Ulm who operated between 1610 and 1626 upon 2000 cases of stone in the bladder and hernia, who was absolutely opposed to operating for stone in several sittings.

Perhaps the most famous work of Hildanus was one upon Gangrene, Hot and Cold, published in 1593, in which he advises that operation must be done by all means in sound tissue and if the gangrene be in the foot the amputation should be 4 to 5 fingers' breadth below the knee. If the gangrene be above the knee, as near as possible to the gangrenous part. He dwells much on the preparation for the operation by purgatives, by supporting the heart's action and sometimes by venesection. He advises that arteries be tied only in strong and full-blooded individuals. At that time, Harvey's discovery of the circulation of the blood had not been made, and the tourniquet was not used. Pressure forceps, which had narrow beaks, were used to compress arteries. When arteries were ligated we have the authority of Meyer Ahrens for the statement that this was done by applying ligatures over artery forceps. After the amputation, compression was applied to the parts.

In an essay "De Combustionibus" he makes 3 degrees of burns, and in treating of gunshot wounds he discusses the problem, whether or not we ought to take into consideration the heating of the bullet by its passage out of the gun, or in passing through the air, or whether a poisoning of the wound takes place from the gunpowder used.

A Latin edition of his works was published in Frankfort, 1646.

WORK OF FABRICIUS HILDANUS.

His works are mostly in Latin, some in French and a few in German.

His best known work that on Gangrene is in old French and was written in 1597. Accurate language was not then the fashion, and more stress was laid on regimen then, than now. His work on stone in the bladder has this title: "Lithotomia Vesicæ, that is, an accurate description of the stone in the bladder, showing the causes and pathological signs thereof, and chiefly of the method whereby it is to be artificially taken out, both of men and of women, by rectum. Written first in High Dutch by Guilhelmus Fabricius Hildanus; first translated into Latin by his Scholler and Communer, and now done into English by N. C. for the general good of the nation and particular use of the Society of Barber Surgeons, London, 1640."

"To the worshippful Companie of the Barber Chirurgians, John Norton wisheth encrease in skill, fortunateness in practice, and all other happinesse. How dangerous in practice the Curation of the Stone by section is, it is evidently evinced not only by reason, if we consider the structure and temperature of the part affected, but by experience also; seeing so few attempt it, and so many doe die who submit themselves to this manner of curation, although the operator perform his part; wherefore too great caution cannot be had in going about this operation."

Chapter 1st of this work by Hildanus begins thus: "The divine Hippocrates, Father of Physicians, hath not without cause in his book 'De Arte,' left us this aphorisme: 'The Physician which can discover the disease, may be able also to cure it, advising thereby all prodent sonnes of art that they should use all diligence and care to get an exact and accurate knowledge of the disease before they intend or think to prescribe an order for the cure.'"

He then advises surgeons to read up, "first the ancients, Hippocrates, Galen, Paulus, Aegineta, but the later writers also, Vesalius, Fallopius, Aquapendente, Ambroise Paré and others, to find out the theory and intention," for he says: "This advise I doe not causelessly set downe in the enhance of this translate, For I know there are some giddy headed and unadvised chirurgians which upon each slight signe and uncertaine suspitian of the stone commonly apply the incision knife to the bladder, boring and searching there, yet in the end, find no stone at all." Again to define a stone he says: "I say the stone is a preternatural, grosse, slymie, coagulated humor, brought into a stone of a thick matter, by a preternaturell heate and hidden quality of the bladder."

CHAPTER 2.

"Because every faithful Chyrurgion and Physitian is, bound before God the Chief Physitian, not only to cure the sick, but by his good councel to keep those that are cured in their health; not only to take away the stone, but to provide against the breeding of any new ones; therefore it is required principally that the Chyrurg know and be taught how and from what causes the stone in the Body of Man and especially in the Bladder, is generated and coagulated together."

He thinks that those who cut men for stone and find none, should be severely punished "and to be paid in their own

coyne, for it is written 'an eye for an eye and a tooth for a tooth;'" also "Besides all this it is chiefly required that the Lithotomist and Cutter of Ruptures should be well versed in the Anatomical part of physick."

We see that Hildanus was an advocate of the higher education of physicians and of their divine right to practice, by the following: "In which words the scripture doth distinguish who are lawfully called to this work and approved by the learned from those who not after the wonted manner enter in at the gate, but like thieves creep in at the windowes and back doores, and by whom the sick men are deprived of their health with their goods and estate.

Such are idle and unskilled Mountebanks, Juglers, vagabonds, executioners, and other detestable villanes of this sorte, whom many would scarce trust for a farthing, whereas in the meantime they trust them with their health, both of their body and soule; So farre the Divell hath blinded man."

"Who so ever therefore should be ungratefull to a faithfull and industrious Physitian, being ordained by God, whether in word or deed, much more by keeping back his reward (of which sort I have met with many) he may easily perswade himself that God will be avenged of him for the labour and trouble which the godly, honest and faithfull Physitian hath undergone for the sick mans sake."

Just before operation "the help and assistance of Almighty God is first to be seriously and devoutly implored by a lawful Minister (if any be present) or in his absence by some of the bystanders who if he please may use one of the prayers prefixed before my treatise De Gangrena et Sphacelo."

The patient is then to jump, or if an infant it is to be shaken, "that the stone may fall down toward the neck of the bladder."

Hildanus advises a perineal lateral operation, and not to attempt to remove a large stone, but to abstain from operation where the patient has no chance of surviving, "for this is better and more commendable in a faithful and diligent Chyrurg than (as some usually doe) to draw the languishing Patients as it were to the shambles."

He relates one of his surgical experiences as follows: "It so befell me at Paterniam when I was about to cut off the thigh of a man of forty yeares of age, and ready to use the saw and cauteries. For the sick man no sooner began to roare out, but all ranne away except onely my eldest sonne, who was then but little and to whom I had committed the holding of the thigh for forme onely; and but that my wife, then great with child, came running out of the next chamber and clapt hold of the Patients Thorax, both she and myself had been in extreme danger."

He then discusses the folly of employing diuretics before the operation.

If we summarize the character and work of Hildanus we see in him a very talented yet modest man of strong vitality and convictions, exceedingly industrious, truly religious, devoted to his profession, restless and migratory in his instincts; a man of great personal magnetism, who by his numerous intelligent observations and skillful operations, more than all his predecessors is entitled to be called the Father of German Surgery.

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THE IMPORTANCE OF TESTING THE OCULAR MUSCLE BALANCE FOR NEAR, AS WELL AS FOR DISTANT VISION.

By Samuel Theobald, M. D.,

Clinical Professor of Ophthalmology and Otology, Johns Hopkins University; Ophthalmic and Aural Surgeon to the Johns Hopkins Hospital, Baltimore.

With increasing experience in dealing with asthenopic eyes, I am more and more impressed with the importance of making in every such case a careful test of the muscle balance for near, as well as for distant vision.

Although in recent years so much attention has been paid to anomalies of the ocular muscles, the significance of the muscle balance in near vision does not seem to have received the recognition which its importance demands. The fact that there is often marked discordance between the behavior of the muscles in distant vision and in near vision appears not to have impressed itself upon systematic writers upon diseases of the eye; and, indeed, it is evident that not all of them are informed as to what is the normal behavior of the muscles when tested for the reading distance.

What constitutes orthophoria in distant vision everyone knows; but, in spite of the fact that it was long ago pointed

out, everyone, it would seem, does not know that, as determined by the vertical diplopia test, the normal state at 12 or 13 inches is an exophoria of 2° or 3° or even of 4°, and that a muscle balance which in distant vision indicates orthophoria is indicative really of a heterophoric condition when found at the reading distance.

In my papers upon "Subnormal Accommodative Power"[1] I have emphasized this point, and have also set forth what, as I view it, is the peculiar significance of esophoria which is present in near vision only, or which is more pronounced in near than in distant vision.

The results which I have obtained in this condition, to which I gave the name subnormal accommodative power, by following the rules laid down in my papers—prescribing at times for young asthenopic emmetropes convex glasses of considerable strength for near work, and for young hypermetropes stronger glasses for near than for distant vision or combining with their near lenses esophoric prisms—have been so eminently satisfactory that this practice is now as much a matter of course with me as the correction of astigmatism or of hypermetropia itself.

The opposite condition, in which there is present a considerable amount of actual exophoria at the reading distance, with normal muscle balance in far vision, a condition by no means rare, is of scarcely less importance, and calls as emphatically for glasses especially adapted for near work, that is to say for lenses which, in addition to correcting such refractive error as may be present, take into account the muscular fault.

Occasionally, in dealing with this condition of discordance between the far and near muscle balance, and having in mind the convenience of the patient, I prescribe bifocal lenses; and, when they see one of my, perhaps, fifteen- or sixteen-year old patients thus equipped, some of my brother oculists are doubtless not a little surprised.

It is not my present purpose, however, to dwell upon these differences of lateral muscle balance to which I have alluded. It was the observation recently of several cases of hyperphoria, which was present in near vision only, and which proved to be an important factor in the causation of the asthenopic symptoms, that prompted me to write this paper.

Thanks to Maddox, we are able now to detect the existence of hyperphoria, and to determine its degree, much more easily and exactly than was formerly possible. With the aid of his multiple rod, and with the further assistance of Dr. Schild's well-contrived little electric light,[2] which I have the pleasure of showing you, I now find it no hardship to test for this defect in near as well as in distant vision. And the outcome of this is, I have learned that differences exist between the vertical muscle balance in far and in near vision much oftener than I had supposed. Indeed, I have not only found cases such as I have mentioned, in which hyperphoria was present in near vision only, but I have met with a few instances, not, however, marked in degree, in which there was hyperphoria in one direction in distant vision and in the opposite direction in near vision—a right hyperphoria, for example, at 20 feet and a left hyperphoria at the reading distance.

I am, therefore, as I said at the outset, more than ever convinced of the importance, in every case of asthenopia, of testing the muscle balance for near vision. Frequently this test shows nothing that is significant; but, on the other hand, it occasionally reveals a fault which must be taken into account if our patient is to obtain complete relief.

I may add, in conclusion, that in determining the balance of the muscles in near vision I use the simplest contrivances—for the vertical diplopia test, a prism of 7° taken from my trial case, and upon a card attached to a rod 12 inches in length a small object calculated to stimulate accommodation, such as an asterisk; and for discovering hyperphoric faults, a multiple Maddox rod with a Schild electric light. The Schild light, if one wishes, may be used instead of the asterisk in the vertical diplopia test; but I do not feel quite sure that it prompts the patient to accommodate as accurately as the asterisk does.

The employment of these tests, which usually give entirely trustworthy results, requires but a very few moments, and the information which they afford is, I am sure, much too valuable to be ignored.

[1] Trans. Am. Ophthalmolog. Soc., 1891 and 1894.

[2] Described in the Ophthalmic Record, June, 1904.

INFANTILE PARALYSIS OF THE ABDOMINAL MUSCLES: WITH REPORT OF A CASE.[1]

BY WM. BURGESS CORNELL., M. D.,

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The commoner distribution of the residual muscular palsies in acute anterior poliomyelitis of infants is too well-known to justify repetition. Nearly every monograph or text-book on the subject gives tables showing the relative frequency of the muscular involvement, but very few consider the question of the abdominal muscles. In looking over the literature, so few cases have been found as to justify the conclusion that a residual paralysis of the abdominal muscles in infantile paralysis is rare.

It is a matter of common record that the paralysis at onset is more widespread than at any subsequent time. On this account, coupled with deficient observation, it is possible that

[1] From the Neurological Dispensary, Johns Hopkins Hospital.

many cases showing participation of the abdominal muscles are overlooked. This seems the more probable when we consider the statement made in many text-books that the trunk muscles, though often paralyzed at first, rarely remain so, together with the fact that, especially in dispensary practice, the patients are not seen for some days or weeks after the onset. In the absence then of adequate data on the occurrence of abdominal involvement in the initial paralysis we may provisionally state that if frequent, the tendency in the vast majority of cases is to rapid recovery. The rarity of a residual paralysis in this region may be judged from a consideration of some of the monographs on infantile paralysis.

Seeligmüller (1) in his series of 75 did not have a case of either back or abdominal paralysis.

Sinkler (2) gives in his 340 cases 22 as having involvement of "trunk," none of these, I am informed, included abdominal muscles, but showed impairment only of the muscles of the back, which in every instance was temporary.

Starr (3) in his text-book makes only passing reference to the subject, but gives 4 in his series of 117 cases which showed involvement of "trunk." He believes probably one-third of the trunk cases have paralysis of the abdominal muscles. He has seen 6 such cases, but I am not informed whether they were temporary or permanent. I have been able to collect the following cases which resemble more or less the one I report.

Duchenne fils (4) in his series of 75 cases mentions one a boy of 10 months, who 6 months previously had a generalized paralysis. The movements returned to the upper extremities, but the legs showed a flaccid paralysis in most of the muscles. On the right the muscles of the abdomen and trunk were for the most part atrophied, giving a dorsal scoliosis with convexity to the right. The abdominal walls on the affected side were thin and gave no response to electrical stimulation. When the infant cried there was contraction only on the left, while on the right the abdomen bulged out in a hernia-like prominence. The child was lost sight of and the final outcome was not learned. Duchenne states, "this observation of atrophic paralysis of the muscles of the trunk and abdomen is the only one I know of, and I have not been able to find a similar one in the literature on the subject."

Birdsall (5) has reported one case in which the paralysis was also unilateral.

Bernheim (6) and Leiner (7) have each described one. The former, one of the oblique muscles; the latter, a case very similar to mine, except that the patient was 12 years old.

In the large number of cases of poliomyelitis seen at the Johns Hopkins Hospital Dispensary, the following is the only one, so far as I am aware, showing a residual paralysis of the abdominal muscles. The case lends an additional interest in that it presented the crossed type of paralysis of the extremities, which appears only in a very small proportion of the cases.

Isaac H., Russian Jew; aet. 21 months; admitted to the Johns Hopkins Hospital Dispensary, August 6 (No. C62260). The family history is negative. The child was said to be healthy until present attack. From appearances he must have been surrounded by squalid conditions. Two weeks previous to admission or about July 23, he had an attack of fever lasting three days. During this time the child slept almost constantly. Afterwards it was noticed that the infant could not sit or stand, and that the right leg and left arm were paralyzed. By August 9 the movements had returned to both affected members, the hand to a less degree. By August 20 the child could walk, using both arm and leg fairly well. No note was made on the condition of the abdomen prior to September 15 when the paralysis was first noticed. There must have been asymmetry from the first, which became more apparent as the muscles grew more flaccid and atrophic. November 15. *Present Condition.*—The child is fat and healthy looking, complexion ruddy. Weight 27.5 pounds, height 31 inches, head, occipto-frontal circumference, 19.7 inches (Holt gives 26.5, 32.5, and 18.9 as corresponding figures for a boy of 2). The head is somewhat square-shaped, with undue prominence of frontal and parietal eminences, while the vertex tends to flatness. Chest is well-formed, symmetrical, and expands equally both in quiet and deep breathing. The diaphragm and intercostals are normal. There is no rickety rosary; no bracelets. There are no visible signs of paralysis in arms or legs except the left arm seems slightly smaller and measures 0.5 cm. less than the right, at its middle point. The forearms measure alike. The biceps tendon, radial biceps, ulnar and triceps reflexes are present, equal and normal. The thighs and legs measure alike. The knee-jerks are lively and equal. Tendo Achillis reflex normal. Scratching the soles of his feet produces flexion of all the toes and of the foot, alike on both sides. It is difficult to test accurately the relative muscular strength, but all movements in arms and legs seem symmetrically strong. The infant walks well, but favors the right leg somewhat, rotating it outward so as to step off the inner side of foot.

Abdomen.—The relative hepatic dulness begins 3 cm. above the costal margin and extends 8 cm. downward in nipple line. In mid-line by dipping, it extends 8 cm. below the ensiform bone. Spleen is palpable. Palpation and percussion are otherwise negative. In dorsal decubitus the abdomen is full, but is more prominent on the right. Abdominal skin reflex is present on left, absent on right. Umbilicus is in mid-line. As the child cries and raises the intra-abdominal pressure, the right side balloons out very markedly. On palpation the muscles may be felt to contract under the hand on the left, but not on the right side. In the erect position the conditions are intensified. The left abdomen is now seen to be quite prominent. (Patient's sister states that the belly was quite large before the illness, and we may infer a mild previous rickets.) The asymmetry is much more evident in this position, and as the child cries, the right side balloons out to the full limit of the flaccid and paralyzed wall. Fig. 1 shows this condition in profile. Fig. 2, as well as Fig. 1, shows the greatest protrusion is in the lower right quadrant. Fig. 3 is a profile of the left side, the child is sobbing, which amounts



FIG. 1.—Maximum protrusion in profile.



FIG. 2.—Maximum protrusion, three-quarters face.



FIG. 3.—Profile of left side.

ERRATUM.—This plate should have been inserted in the BULLETIN for January, 1905, opposite page 12.

for the indistinct outlines and gives this side a somewhat fuller appearance than in reality. The paralyzed muscles are the obliqui; the transversalis, and half of the rectus abdominis on the right. An attempt was made to test their electrical reactions, but as the child unfailingly cried every time the current was applied, nothing definite could be learned. As the pictures show, there is no lordosis. There is, however, a slight scoliosis in the lumbar region, with convexity to right.

In conclusion I wish to thank Dr. Thomas, from whose clinic I report this case, and Dr. Cushing for kind help.

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THE DIAGNOSTIC VALUE OF TUBERCULIN IN ORTHOPEDIC SURGERY.

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For the permanent cure of tuberculosis in any form we must be able to recognize the presence of the disorder while it is still in its incipiency. Any means, therefore, which will afford us an opportunity to attain this end at an earlier date than ordinarily we are accustomed to do, will go far toward lessening the death rate, will increase the percentage of cures, and cannot fail to be of the greatest benefit to mankind.

Koch (1) in 1890 described such an agent in tuberculin, and in his earliest articles (2) definitely stated its diagnostic, as well as its therapeutic value. But amid the enthusiasm of the medical profession over a discovery that produced a specific for the cure of tuberculosis, practically no attention was at first paid to its diagnostic properties. Year by year, however, despite the disfavor into which it speedily fell as a therapeutic agent, tuberculin has gradually pushed its way to the front again until today it is recognized as one of the most important diagnostic agents in beginning tuberculosis.

We do not propose in this paper to speak of its therapeutic or diagnostic properties in incipient pulmonary or glandular tuberculosis. Much has been written on these subjects by Fränkel (3), Mettetal (4), Casselbery (5), Finkler (6), Guttman, Otis (7), Trudeau (8), Tinker (34), and others. Here we would rather refer to the results in a series of cases which, we believe, go to show the great value of tuberculin as a means of diagnosis in bone and joint tuberculosis. Take, for instance, disease of the spine. In very early cases how many of us are there who have not too often been in doubt whether we were dealing with tuberculosis, rachitis, rheumatism, syphilis, spondylitis deformans, or simply a sprain? Is it not sometimes difficult in diseases of the hip to differentiate tuberculosis from synovitis, gonorrhœal arthritis, rheumatism, osteo-myelitis, coxa vara, or fracture? The same may be said in disease of the knee, ankle and other joints. We are fully convinced that in the proper use of tuberculin we have a perfectly harmless method, simple in its application, which will almost invariably tell us of the presence of tuberculosis long before it can be detected by any other means; nay more, tuberculin not only shows us that we are dealing with a tuberculous process, but also in the great majority of instances points out the location of the focus.

The tuberculin used by us came from the laboratory of Dr. Trudeau, to whom we are greatly indebted for a liberal supply. His manner of preparing it is very similar to that of Koch. The tuberculin is a 50 per cent glycerine extract of the bouillon on which the tubercle bacilli have been grown. The flasks are inoculated from a well developed culture of actively growing bacilli, and are then kept in the incubator for six weeks at a temperature of about 37° C. For the tuberculin the contents of flasks are chosen which show a well developed growth over the surface of the bouillon. From one liter of these about 100 cc. of tuberculin are procured. The cultures, being boiled for fifteen minutes, are filtered through paper; the fluid is then put in a porcelain vessel and boiled slowly down to the required concentration (usually 1/10). This concentrated remainder is then passed through a Berkefelder filter. The filter is thoroughly cleansed before and after each filtration and the tuberculin is passed through while it is moist from its last cleansing with sterile water. We have now obtained our stock solution. For injection this solution is mixed with ½ per cent carbolic acid solution, so as to give the strength required and should always be freshly made.

Our mode of applying the test is as follows: The temperature of the patient is taken every two hours for a period of

twenty-four hours preceding the injection. The ordinary hypodermic syringe is used with a needle slightly longer than usual. The needle is inserted deep into the deltoid muscle, thorough aseptic precautions being observed. The puncture wound is covered with sterile gauze, which remains on for twenty-four hours. The temperature is taken every two hours for the ensuing 24-48 hours. If the time selected for the injection be between 8 p. m. and midnight, we can neglect the temperature until 6 a. m. the next morning, as the reaction does not begin until six or eight hours later and the patient need not be disturbed during the night. If possible, the temperature during 24-48 hours preceding the injection should be normal. If, however, pyrexia is present during this period, a positive reaction is still recognizable by means of the local signs. A rise of at least 2° F. is required to constitute a temperature reaction. Using this method, we have injected at their homes forty patients in private practice and from the orthopedic dispensary clinic at the Johns Hopkins Hospital. A synopsis of these cases with their reactions will be found in the following table:

this test has been applied in the wards of the Johns Hopkins Hospital where tuberculin has been employed continuously for the past six years. In looking over the series of cases we find that twenty-five gave a positive and fifteen a negative reaction. Of the twenty-five patients in whose cases a positive reaction was obtained, six were subsequently operated on and all proved to be tuberculous. In eighteen of the remaining nineteen cases the diagnosis has been verified by the subsequent history and response to treatment. The only remaining case, while proven to be tuberculous by its positive reaction to tuberculin, both general and local, is of such recent date that the subsequent history is not as yet available. In regard to the fifteen patients who did not react, one was operated upon and no evidence of tuberculosis was found; of the other fourteen, eight have recovered under non-tuberculous treatment; the remaining six are improved and all suspicion of tuberculosis has been removed. Radiographs were taken of fifteen out of the twenty-five cases which reacted to tuberculin. Of these fifteen cases, six showed a focus, in five the disease was suspected only, and four showed no lesion. The

Case.	Radiograph.	Provisional Diagnosis.	Tuberculin.	Diagnosis.
1. W. F., æt. 1½ years...	No	Potts disease	Mgm. 1.5. Mgm. 3.5, positive	Potts disease
2. W. M., æt. 32 years ...	No	Potts disease	Mgm. 2. Mgm. 4, negative	Syphilitic spine
3. W. M., æt. 16 years ...	No	?	Mgm. 1, negative	Osteo-arthritis spine
4. W. M., æt. 37 years ...	Yes	?	Mgm. 5, negative	Osteo-arthritis spine
5. W. M., æt. 24 years ...	Yes	Potts disease	Mgm. 3. Mgm. 5, negative	Osteo-arthritis spine
6. W. F., æt. 3 years.....	No	Rachitis	Mgm. 2, positive	Potts disease
7. W. M., æt. 8 years	No	Potts disease	Mgm. 2, positive	Potts disease
8. W. M., æt. 25 years ...	No	Scoliosis	Mgm. 2. Mgm. 6, negative	Scoliosis with sciatica
9. W. M., æt. 16 years ...	No	Potts disease	Mgm. 5, negative	Osteo-arthritis spine
10. W. M., æt. 5 years	No	Tuberculosis of hip joint	Mgm. 2, positive	Tuberculosis of hip joint
11. C. M., æt. 10 years....	Yes	Tuberculosis of hip joint	Mgm. 3 and 4, positive	Tuberculosis of hip joint
12. W. F., æt. 12 years....	Yes	Effusion into joint	Mgm. 5, positive	Tuberculosis of hip joint
13. W. M., æt. 3½ years...	Yes	?	Mgm. 3, positive	Tuberculosis of hip joint
14. W. F., æt. 7 years.....	Yes	?	Mgm. 5, positive	Tuberculosis of hip joint
15. W. M., æt. 8 years	Yes	?	Mgm. 5, positive	Tuberculosis of hip joint
16. W. F., æt. 16 years....	Yes	?	Mgm. 3, positive	Tuberculosis of hip joint
17. W. M., æt. 17 years....	No	Effusion into joint	Mgm. 2, negative	Effusion into joint
18. W. F., æt. 29 years....	No	?	Mgm. 2 and 5, negative	Sciatica
19. W. M., æt. 15 years ...	Yes	Fracture	Mgm. 3 and 4, positive	Tuberculosis of hip joint
20. W. M., æt. 12 years ...	Yes	Tuberculosis of hip joint	Mgm. 3 and 5, negative	Coxa-vara
21. W. M., æt. 5 years.....	No	Coxa-vara	Mgm. 1 and 3.5, negative	Coxa-vara
22. W. F., æt. 3 years.....	No	?	Mgm. 1.5 and 2.5, negative	Synovitis of hip
23. W. F., æt. 32 years....	Yes	Tuberculosis of both hip joints	Mgm. 2, positive	Tuberculosis of both hip joints
24. W. M., æt. 6 years	Yes		Mgm. 3 and 6, negative	Coxa-vara
25. W. F., æt. 43 years....	No	Tuberculosis of hip joint	Mgm. 4, positive	Tuberculosis of hip joint
26. W. M., æt. 12 years ...	No	Tuberculosis of hip joint	Mgm. 3, positive	Tuberculosis of hip joint
27. W. F., æt. 4 years.....	No	Tuberculosis of hip joint	Mgm. 2.5, positive	Tuberculosis of hip joint
28. W. M., æt. 6 years.....	No	Tuberculosis of hip joint	Mgm. .5, positive	Tuberculosis of hip joint
29. W. F., æt. 3 years.....	Yes	Tuberculosis of hip joint	Mgm. 1, positive	Tuberculosis of hip joint
30. W. F., æt. 30 years....	Yes	Gonorrhœal rheumatism	Mgm. 5, positive	Tuberculosis of hip joint
31. C. M., æt. 9 months...	No	Tuberculosis of knee joint	Mgm. 1.3, positive	Tuberculosis of knee joint
32. W. F., æt. 16 years....	Yes	?	Mgm. 3 and 5, positive	Tuberculosis of knee joint
33. W. M., æt. 10 years ...	Yes	Tuberculosis os knee joint	Mgm. 2.5, positive	Tuberculosis of knee joint
34. W. F., æt. 23 years....	Yes	Chronic synovitis	Mgm. 5, negative	Chronic synovitis
35. W. M., æt. 10 years....	Yes	?	Mgm. 2 and 5, negative	Chronic synovitis
36. W. F., æt. 8 years.....	Yes	Tuberculosis of ankle joint	Mgm. 5, positive	Tuberculosis of ankle joint
37. W. F., æt. 4 years.....	Yes	Tuberculosis of ankle joint	Mgm. 2, positive	Tuberculosis of ankle joint
38. W. F., æt. 20 years....	Yes	Old fracture os calcis	Mgm. 4, negative	Old fracture os calcis
39. W. M., æt 2 years.....	Yes	Green stick fracture tibia	Mgm. 3, positive	Tuberculosis of lower end of tibia
40. W. F., æt. 21 years....	Yes	Tuberculosis of ankle joint	Mgm. 3, positive	Tuberculosis of ankle joint

These cases were selected almost invariably in order to clear up the diagnosis. Our results show the ease with which tuberculin may be used in private practice and the accurate data that can be obtained under such circumstances. We have not included here the large number of cases in which reasons for this will be discussed later. For convenience we have arranged the patients in groups according to the joint involved. A few cases of especial interest will now be discussed briefly.

Case 1. White; female; aged one year and six months;

admitted to the clinic January 10, 1900. Three days before she had a slight fall. Although she had previously walked for four months she now prefers to crawl; cries and is fretful. Examination showed only a slight restriction to hyperextension of the back; no kyphosis. Seat of pain not to be located. Two physicians connected with the dispensary had seen her just before admission, one suggested rachitis of the spine; the other malnutrition. Two injections of tuberculin were given. The first (1.5 mgm.) was followed by a rise of temperature to 100° F. The reaction was considered suggestive. A few days later 3.5 mgm. were given, and seventeen hours later the temperature was 100.5° F., having been normal previous to the injection. The child refused nourishment, and was very restless. On examination of the back, the resistance to hyperextension was greatly increased; the child refused to stand; the knee-jerks were increased. Here then was a positive reaction both general and local. On the following day the temperature had returned to normal and the general and local signs were exactly as those which had been present previous to the injection. The child was treated for Pott's disease with plaster jackets and a Taylor back brace. The note of her condition three years after the beginning of treatment is as follows: "The child is practically well with a slight kyphosis of the third lumbar vertebra, having passed through a typical Pott's disease during this period."

In this case tuberculin gave us a positive diagnosis at a time when the clinical symptoms were not sufficient to warrant a positive decision, and allowed treatment to be instituted in time to prevent deformity.

On the other hand, the negative value of tuberculin is shown in the following case:

CASE 2. White; male; aged thirty-two; admitted to orthopedic clinic October 5, 1901. Referred by the nervous clinic with a diagnosis of tuberculosis of the spine. *Family history,* negative. *Previous history.* Lues ten years ago. *Present illness.* The patient has complained of pains in his back radiating to the abdomen for the past five months. The pains are present during the day and night. The back is becoming stiff in the lumbar region, and the patient finds it difficult to pick up objects from the floor; there has been a continuous loss of strength, and the man is not steady on his feet. Loss of weight, fifteen pounds. *Examination:* The patient walks with an unsteady gait; holds his back perfectly rigid. There is some obliteration of the lumbar curve, but no actual kyphosis. The knee-jerks are markedly increased. Ankle clonus is present. There is considerable pain attending a jarring of the heel. A probable diagnosis of tuberculosis of the spine was made and the patient was treated by means of plaster jackets for the first few weeks. He thought he improved a little; but later the pain grew worse at night. The symptoms of paralysis increased and the man lost weight rapidly. For six weeks we persisted in the treatment, but the patient gradually grew worse. On December 28, 1901, he was given 2 mgm. of tuberculin. There was no general or local reaction. On December 30, 4 mgm. were given. No reaction followed, either general or local. This caused us to change our diagnosis and for the first time to think seriously of his specific history as an etiological factor. Treatment with inunctions and potassium iodide internally was then begun. Within a month the patient gained three pounds in weight; the pain ceased almost entirely; no ankle clonus could be obtained and his knee-jerks became far less lively. He continued to wear a laced plaster jacket as a means of support. On May 1, 1902, four months after the initiation of the syphilitic treatment, he felt perfectly well; no brace was worn; the back was not stiff; all symptoms had disappeared. Fifteen months after beginning the treatment, he reported for observation and seemed well in every respect. Specific treatment, however, was continued. This case shows the value of tuberculin in eliminating tuberculosis and arriving at the true etiological factor.

Again let us contrast two cases of disease of the hip-joint.

CASE 13. Boy; white; age 3½ years; admitted to the orthopedic clinic March 3, 1903, complaining of a slight limp. Mother died of pulmonary tuberculosis. He had had diphtheria two years previously. *Present sickness.* Four months ago he had a slight fall on the floor while playing and since that time has had a limp which has slightly increased. There are no other subjective symptoms. Examination shows a slight limp. There is an apparent shortening of ½ cm. No other deformity. Possible flexion of 85° and possible abduction of 30°. No resistance to hyperextension, adduction, internal or external rotation. No muscle spasm. Very slight atrophy of thigh and calf.

In this case the diagnosis was not plain; it was by no means a well defined case of tuberculosis of the hip. The radiograph showed that the distance from the trochanter to the head of the femur was slightly less than on the other side. There appeared to be a slight roughness of the acetabulum and the trochanter possibly showed a slight rarefaction.

On March 25, 1903, at the patient's home, 3 mgm. of tuberculin were given in the usual manner. Fourteen hours afterward the temperature had reached 101° F. This was accompanied by loss of appetite and extreme restlessness. All the local signs were decidedly increased. Pain in the hip and knee was complained of. There was distinct muscle spasm. The leg assumed a position of slight flexion and there was a decided limitation of all the motions. On the following day the hip had returned to its former condition and the general symptoms had disappeared. Here the reaction was positive. The radiograph, owing to the age of the child, did not show a definite focus, but under the influence of tuberculin the local signs presented such a definite picture that there could be no doubt as to the tuberculous nature of the affection.

The absence of a positive reaction on the other hand in diseases of the hip of a non-tuberculous character is shown in the following case:

CASE 20. White; male; aged 12 years; admitted May, 1902, complaining of a limp. Family and previous history unimportant. *Present illness.* In October, 1901, the boy was hurt on the thigh while playing foot-ball and began to limp. There was no history of night cries and no pain. He

was put up in a plaster spica and given crutches, which he used for six weeks. A tentative diagnosis of hip disease was made by a prominent surgeon. After the cast was removed he continued to limp. He was seen by us in May, 1902, six months after the original injury, and on examination the leg showed marked outward rotation, slight apparent shortening. Flexion was limited to 60°, abduction to 45°, and no rotation was allowed. No pain and no muscle spasm. The diagnosis was made of slight coxa vara, non-tuberculous in origin. Three and five mgm. of tuberculin were given at an interval of two days with absolutely no local or general reaction. The diagnosis of coxa vara was thus confirmed by a negative reaction to tuberculin and a radiograph, which showed no tuberculous focus, but a slight bending of the neck of the bone. The treatment consisted in massage and passive motion, both of which would have been contra-indicated had the joint been tuberculous. It is now eleven months since he was first seen by us. There is very little limp; the possible flexion is now 90°, possible abduction 80°.

The last case that we will discuss in detail seems to be of particular importance:

Case 32. White; female; aged 16 years, admitted, February, 1903, complaining of pain in the left knee on pressure and while standing. *Family history.* Father and mother both dead of pulmonary tuberculosis. Previous history, unimportant. *Present sickness.* Three weeks ago she had a slight fall while skating, to which no attention was paid. Since that time there has been a slight limp. The only symptom she presents is pain on pressure over the patella. There are no other local signs of disease. On February 3, 1903, she was given 3 mgm. of tuberculin. Eighteen hours afterwards the temperature had reached its maximum of 100.8° F., after which it rapidly fell to normal. There were general symptoms of nausea, headache and loss of appetite. Of greater importance we think were the local signs, for, whereas before the injection, there was only pain on pressure over the patella, there was now a slight rise of local temperature; the motions were restricted in extreme flexion and extension, and even the slightest pressure over the patella would cause exquisite pain. On the following day the temperature was normal; the general symptoms had disappeared and there remained locally only the slight pain as before the injection. The radiograph showed a slight focus of disease, about 1½ cm. in length and ½ cm. broad, situated in the internal condyle, running toward the joint. The tuberculous nature of the disease having been so early established by means of the tuberculin, and its extent ascertained by radiography, it was decided to see if the focus could not be removed and a stiff joint avoided. Accordingly the joint was opened for inspection, and on the top of the internal condyle directly under the patella a circumscribed raised area of inflammation was found about 1½ cm. in diameter, which showed, however, no tubercles to the naked eye. This area was left alone, the joint was closed, the area of diseased bone immediately beneath this seat of inflammation was removed (extra-articular) and proved to be tuberculous. The leg was then put in plaster. Three weeks later pressure over the patella elicited no pain and the motions of the joint were found to be good.

This case illustrated exceptionally well the diagnostic value of tuberculin in the earlier cases of tuberculosis. In this instance its employment rendered operative interference possible without the destruction of the function of the joint.

As a rule, when tuberculin is given, definite general and local signs are present whenever tuberculosis is present, and are generally absent whenever tuberculosis is absent. The smallest focus of tuberculosis will give a positive reaction and hence the diagnosis can be cleared up at a much earlier date than is possible by any other means.

During the twelve years that tuberculin has been used the dosage has varied with different observers. This in itself accounts for the failure in numerous instances to detect the presence of tuberculosis. Such small doses were used that small foci did not give either a general or a local reaction. Grasset (9) says that 2/10 to 5/10 mgm. are useful, while White (10) reports that doses of 1 to 2 mgm. are not to be relied upon. Mettetal (4), using tuberculin in children, gives doses from .1 to .5 mgm. On the other hand, if the dose be too large, even normal individuals may react. According to Koch (11), 10 mgm. may cause such a reaction. He obtained a reaction in himself with a dose of 25 mgm. Often such small doses were given in quick succession that a tolerance was created against a larger dose. So varied are the factors on which the dosage depends, the age of the patient, the seat of the focus, the strength of the tuberculin, its deterioration, and individual susceptibility, that no hard and fast rule can be given. Madison (12) in his recent article follows an initial dose of 4 mgm. by 7 to 10 mgm. when necessary. It has been our custom in small children to give an initial dose of ½ mgm. followed at intervals of two days with 2 two 4 mgm., when necessary. In older patients, 2 mgm. are used as an initial dose, followed in two days by 4 and 6 mgm. as a maximum. In no case have we found it necessary to give more than 6 mgm.

As to what constitutes a positive temperature reaction, all observers are agreed in requiring a rise of at least 2° F. The initial rise generally takes place within the first twenty-four hours and the pyrexia usually lasts over a period of twenty-four hours. The temperature may rise even as high as 104° or 105° F.; the curve of the pyrexia may be atypical, being prolonged over the usual twenty-four for forty-eight hours or more; or the time of the onset may be delayed, but this is due no doubt in most part, as claimed by Madison (12), to deterioration of the tuberculin.

A definite group of symptoms always accompanies the fever; headache, anorexia, nausea, occasional vomiting, restlessness, etc. To those, however, who are dealing with joint and bone tuberculosis the local symptoms are of far more interest and of equal importance. Previous to the injection of tuberculin the local seat of disease should be examined carefully for all signs of the suspected trouble, such as the permanent deformity, possible motions, muscle spasm, local temperature and pain. In response to the tuberculin, if

tuberculosis be present, we shall have all the local signs of the disease distinctly increased, that is, motion will be more limited, deformity will be greater, tenderness and muscle spasm will be exaggerated, and local temperature may be increased; in fact, the local signs alone are so characteristic of a tuberculous process that the diagnosis can be made from these alone.

Koch (1) and Maragliano (13) have laid stress upon the local signs observed in lupus, glandular and pulmonary tuberculosis. Klebs (14) mentions local reactions occurring in disease of the bones and joints, while Fränkel (3) says, "Tuberculin is especially useful in surgical tuberculosis, particularly as in such cases the local phenomena can be so easily observed." On the other hand, Frazier and Biggs (15) are the only observers, so far as we know, who claim an entire absence of a local reaction in tuberculosis of bones and joints. We can only say that in every case that has come under our personal observation the local phenomena, where a positive reaction was obtained, have been of a most pronounced character. The selective action of tuberculin for tuberculous tissue is well recognized, and whenever a patient with a suspected joint gives a general but no local reaction, the probabilities are strongly in favor of the view that the joint in question is non-tuberculous. It is evident, therefore, that the local signs should be carefully observed, as well as those of a general character, in order to definitely locate the tuberculous process.

Is the use of tuberculin harmful in its effects?

A few months after its discovery, Virchow stated that in his opinion it might be harmful. This view has been concurred in by Ambler (16) and Knopf (17) on theoretical grounds. Head (18), Heron (19) and Ewald (20) have reported cases in which very weak patients have died after a large injection; but the evidence is by no means conclusive that death was due to the injection.

On the other hand, the great majority of observers, among whom may be mentioned Fränkel, Mettetal, White, Lathan (21), Neff (22), Osler (23), Klebs, Martin and Robbins (24), France (25), Elder (26), and Voges (27), are unanimous in their statements that, when tuberculin is used in proper doses, there are no harmful effects. We have never seen a case in which any permanent damage had been done by tuberculin. A dose which is too large may produce a fever that is prolonged beyond the usual twenty-four hours, and the local signs may persist for a longer time than usual, but within a day or two the temperature always returns to normal and the local signs become similar to those before the injection.

Is tuberculin a specific in the diagnosis of tuberculosis?

According to some observers, syphilis, leprosy and actinomycosis react to tuberculin. Mettetal (4), Billroth (28) and von Eiselsberg (29) have seen cases of actinomycosis which gave a positive reaction, but Mettetal definitely states that the reaction was atypical. Goldschmidt (30), Babes and Kalendro (31) state that leprosy may react. In 109 autopsies of lepra reported by Abraham (32), 30 per cent showed tuberculous lesions. It seems highly probable, therefore, that most of the reactions reported in leprosy were due to an accompanying tuberculosis. In regard to syphilis, Beck (33) states that one-half of such cases react to tuberculin, while Otis (7) in 35 cases in which the diagnosis was carefully made, found only 12 per cent that reacted, and he considers Beck's figures as entirely too high. Fränkel, on the other hand, thinks the probability of obtaining reactions in uncomplicated cases of syphilis very doubtful. He reports a case of a syphilitic ulcer, which gave a general, but no local reaction to tuberculin. The ulcer was cured by inunctions and potassium iodide internally, and again the patient gave a general reaction to a dose of 1 mgm. He considers that there he was dealing with syphilis complicated by hidden tuberculosis.

The only patient in our series (Case 2) in whose case a reaction to syphilis was in question, failed to react to 2 and 4 mgm. of tuberculin and entirely recovered under specific treatment. From the cases of syphilis reported by various observers, it seems probable that a small number give a reaction, but further evidence is necessary to show that there is no associated tuberculosis in these cases. Broadly speaking then, it may be said that tuberculin is practically a specific in the diagnosis of tuberculosis.

The radiograph has come to play an enormous role in the work of the orthopedic surgeon. It is one of the most helpful means which we possess to point out lesions of bones and joints and yet it has its limitations, especially in the very cases in which we most need its help. By far the greater number of our patients with bone and joint tuberculosis are children. The structure of their bones and the relatively large proportion of cartilage in such cases does not lend itself to differentiation by means of radiography as readily as in adults. It has often been our experience in children that even when the clinical signs were sufficient to make a diagnosis of tuberculosis, the best radiograph would fail to present a picture of the disease process or would do it so imperfectly as to make us doubt its existence. In such cases tuberculin would invariably give us both a general and local reaction. On the other hand, tuberculin plus the radiograph forms a combination of diagnostic agents which are of the greatest value, especially in adults, as is shown in case 32, where tuberculin gave the diagnosis and the radiograph showed the location and extent of the focus.

The application of the tuberculin test is in reality a most simple procedure, much easier than a blood count and no more difficult than an ordinary injection. Naturally, the method is more accurate in hospital work, owing to the aid of a competent nursing staff, and yet with a little more exertion on the part of the physician, private and dispensary cases need but little more care. The same physician who examines the case before injection should also do so at the height of the reaction. The temperature must be carefully taken and recorded every two hours. It is generally agreed that tuberculin is an unstable product and deteriorates if not kept in a cool, dark place. The ½ per cent carbolic acid solution should be made up freshly before each injection. The majority of observers

agree that it may be used if not kept more than three days. Madison (12) believes that a fresh bottle of the stock solution should be opened once a month. In his opinion the failure of tuberculous cases to react and delayed reactions are primarily due to deterioration of the tuberculin.

The reliability and harmlessness of the test may be judged by the immense number of observations upon cattle where autopsies can be obtained and results verified. Voges (27) in eight thousand autopsies upon cattle has shown that the test is accurate in 90 per cent. Koch, with an experience of three thousand cases, considers the test almost absolute.

Our own work, when taken in conjnction with that of others, would appear to justify the following conclusions:

1. Tuberculin is the best and most reliable diagnostic agent for incipient tuberculosis of bones and joints.

2. Its proper administration is attended by no permanent harmful effects.

3. The dosage is variable and it is rarely necessary to exceed a dose of 6 milligrams.

4. The local signs are of equal, if not greater, importance than the general reaction, in bone and joint tuberculosis.

5. Tuberculosis practically always reacts to tuberculin.

6. Diseases other than tuberculosis may possibly react to tuberculin, but the evidence on this point is not conclusive.

7. The diagnosis of tuberculosis can be made earlier and with more certainty by means of tuberculin than by radiography.

8. The tuberculin test is applicable to private and dispensary as well as to hospital practice.

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For particulars, apply by letter to Dr. E. N. Brush, Physician-in-Chief and Superintendent, Sheppard and Enoch Pratt Hospital, Station "A," Baltimore.

A PRACTICAL METHOD OF DEMONSTRATION.

BY W. J. CALVERT, M. D.,
University of Missouri, Columbia, Mo.

The problem of demonstrating either the normal or abnormal relations of organs has presented many difficulties which have given rise to many devices such as serial sections of the body, schematic drawings, models, etc., all of which are of value, but none of which are entirely satisfactory. In addition many of the larger drawings and most models are expensive and are beyond the reach of many institutions and most individual students.

Wherever practicable full sized drawings are the most desirable as the student then is not required to mentally convert a one-fourth, one-half or a three-fourth sized drawings to one of full size.

For full sized outline drawings the tracing-cloth and blueprint method extensively used by architects and engineers is very satisfactory. Four original drawings are necessary. One each of the anterior, posterior, right and left sides with the outlines of the several organs projected on each are sufficient. From these, full sized outlines of the thorax, abdomen or pelvis, as desired, may be traced in a relatively short time and the outlines of an abnormally placed organ, etc., may be traced in at will. When the tracing-cloth outline is completed, blue-prints can be made for a few cents each by men who are to be found in every city. In this way as many drawings as is desired may be made and each member of a class can afford to buy a blue-print, which, when worn out, may be replaced at little expense.

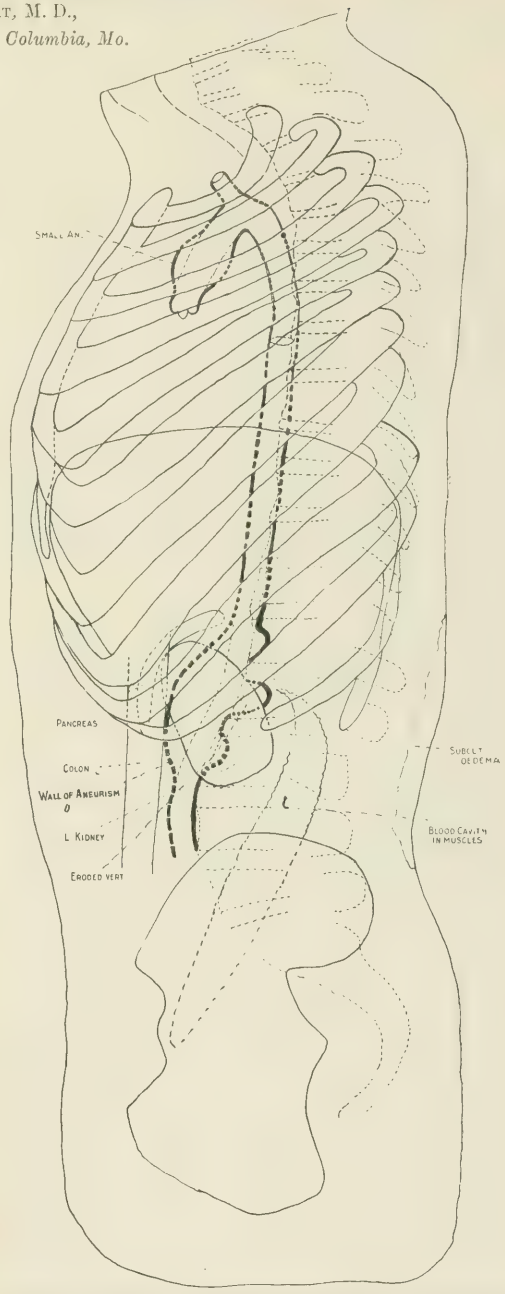
One distinct advantage is that the drawings are not schematic, but are as accurate as measurements allow. In addition they are easily made, cheap, and can be replaced when worn out. They are of especial advantage for demonstrating individual cases to societies, classes and for lecture work.

The materials required are a drawing board, a few thumb tacks, tracing-cloth, india ink and ordinary pens.

If desired, the outlines of the bones or organs may be colored or may be blackened with a soft lead pencil which can be erased later.

From the drawings on cloth, photographs may be easily made for reproduction.

For the original outline drawing of the print which illustrates this article I am indebted to Dr. Potter of the St. Louis University.



Reduced from life size. Heavy black interrupted line indicates lesions.

THE JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read, and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly.

Volume XV is now completed. The subscription price is $2.00 per year. The set of fifteen volumes will be sold for $75.00.

THE EFFECT OF THE BILE UPON THE ESTER-SPLITTING ACTION OF PANCREATIC JUICE.[1]

A PRELIMINARY COMMUNICATION.

By Albion Walter Hewlett, M. D.

(From the Physiological Laboratory of the Cooper Medical College, San Francisco, Cal.)

That the bile assists in the digestion and absorption of fats has long been recognized, but the manner in which it does this has never been fully worked out. The presence of bile favors the emulsification of fats and this indirectly aids the fat-splitting action of the pancreatic juice, because the finer the emulsion the greater is the surface of fat presented to the action of the fat-splitting enzyme. Little regard, however, has been paid to the possibility that the bile might assist the enzyme in any more direct manner. Pawlow[2] indeed asserts that the presence of bile so changes the medium that the fat-splitting proceeds two or three times as fast as it would if no bile were present. Bruno, a pupil of Pawlow, estimates the acceleration of the lipolytic action as ten to twenty times.[3] Glassner, working on pancreatic juice obtained from a human pancreatic fistula, found that the addition of bile to the pancreatic juice increased its action upon olive oil about one and one-half times.[4] The manner in which the bile assisted the pancreatic lipase was not especially considered by these investigators.

At the suggestion of Dr. W. E. Garrey, I have endeavored to ascertain more definitely the effect of bile upon the ester-splitting action of pure pancreatic secretion. The latter was obtained from dogs by means of secretin injections[5] or by injections of both secretin and pilocarpin. In this manner varying amounts, up to forty cubic centimeters, of pure pancreatic juice were obtained from each of a series of dogs and the action of this secretion was tested upon a variety of esters with and without the addition of bile.

Pure pancreatic juice decomposes ethyl butyrate surprisingly slowly if we compare it with the action of pancreatic extracts upon the same ester.[6] If one or two cubic centimeters of pancreatic juice be diluted up to five cubic centimeters with water and if the mixture be allowed to act upon 0.25 cc. of ethyl butyrate for twenty-four hours at 37° C., the difference between the acidity produced and that produced by an equal amount of boiled pancreatic juice is usually about 0.1-0.2 cc. of a 1/20 normal solution, although it may in some instances run up to 1.0 cc. or slightly more. Unboiled bile also decomposes ethyl butyrate very slowly, not differing appreciably in this respect from boiled bile. If the bile be added to the pancreatic juice, however, the cleavage of the ethyl butyrate proceeds with great rapidity and in twenty-four hours an acidity amounting to 7.0-16.0 cc. 1/20 normal solution will be produced. Similar results were obtained when ethyl acetate or amyl acetate were used in place of ethyl butyrate.

The ordinary fats are insoluble in water and they are therefore but little suited to a solution of the problem at hand, because any acceleration in the action of the pancreatic juice, which the bile would cause, might be attributed to its emulsifying action. This difficulty however, is, overcome if a soluble triglyceride, such as triacetin, be used, for then the question as to the degree of emulsification is eliminated. It was found that pure pancreatic juice, even without the addition of bile, splits triacetin much more readily than it does ethyl butyrate, ethyl acetate, or amyl acetate. In one experiment the acidity produced in an hour at 20° C. amounted to 0.5 cc. 1/20 normal solution and in twenty-four hours to 12.6 cc. On the addition of bile, the decomposition proceeded at a much more rapid rate just as it did in the case of ethyl butyrate. The acidity produced in one hour amounted to 13.0 cc. and in twenty-four hours to 18.6 cc. The acceleration, therefore, was very marked during the first hour, and the reason that this acceleration was less apparent after twenty-four hours probably lay in the fact that the reaction was approaching an equilibrium.

The addition of bile also accelerates the action of the pancreatic secretion upon emulsions of olive oil, but to what extent and why this occurs has not as yet been fully determined.

Which constituent of the bile possesses this peculiar property of accelerating the ester-splitting action of the pancreatic juice? Boiling the bile does not destroy this property and we may therefore infer that it is not due to an enzyme. Furthermore, this property resides neither in the cholesterin, in the pigments, in variations in reaction, nor in variations in the amount of calcium salts present. Precisely the same accelerating effects may, however, be produced by the addition of lecithin to the pancreatic juice. Thus in one experiment the pure pancreatic juice by its action on triacetin for twenty-four hours produced an acidity amounting to 4.3 cc. 1/20 normal solution; the same plus two cubic centimeters of bile produced 19.5 cc. acidity, and plus two drops of a strong alcoholic solution of Merck's lecithin produced an acidity of 19.9 cc. A commercial preparation of the bile salts will also accelerate the ester-splitting of the pancreatic juice, but it seems that the more the bile salts are purified, the less effect they have in this respect, so that it is possible

[1] This research has been completed by the aid of a grant from the Rockefeller Institute for Medical Research.

[2] Pawlow: The Work of the Digestive Glands. Trans. by W. H. Thompson, p. 159.

[3] Die Galle als wichtiges Agent bei der Verdauung. Inaug. Diss. St. Petersburg, 1897-98. Ref. in Jahresber. Thier-Chemie. Vol. 27, p. 441.

[4] Ztft. f. physiol. Chem., Vol. 40, p. 465.

[5] Bayliss and Starling: The Mechanism of Pancreatic Secretion. Jour. of Physiol., Vol. 28, p. 325.

[6] Kastle and Loevenhart: Am. Chem. Jour., Vol. 24, p. 491.

that the action of the crude preparation is due to a contamination with lecithin.

Various possibilities present themselves as to the manner in which the bile assists the ester-splitting action of the pancreatic juice. In the first place, does it act by converting a proferment into a ferment, an action analogous to that exerted by the enterokinase of the intestines upon the proferment of trypsin?[7] In considering this question, we must remember that if this hypothesis were true, a small amount of bile would be just as effective as a larger amount provided it acted for a sufficiently long time, and that if sufficiently small amounts of bile were added to the pancreatic juice the rate of cleavage could be shown to progressively increase as more and more of the proferment were converted into the ferment. It was found as a matter of fact that these conditions are not realized in the case of the action of bile upon the pancreatic juice. Another possibility is that there is a substance in the pancreatic juice, itself inert, which combines with some constituent in the bile to form the fat-splitting enzyme. Such a condition would be analogous to that described by Kyes[8] for cobra venom. Alone this exerts little if any hæmolytic action; plus lecithin the action is most marked. The pancreatic juice, however, is moderately active even without the addition of bile. It would, therefore, be necessary to suppose that the pancreatic juice normally contains a trace of lecithin, but that this is not sufficient to render active any considerable portion of the fat-splitting ferment. It seems to us more probable that the bile acts as an accelerator upon the fat-splitting ferment, and indeed this is more in accord with the modern view that all ferment action is in the nature of an acceleration. We know that the esters will slowly decompose in pure water and the same is true if they are placed in boiled pancreatic juice. If the secretion be unboiled, *i. e.*, if the ferment be present, the decomposition proceeds at a somewhat more rapid rate, and if to this, bile be added, the decomposition is still further accelerated. We do not know exactly how this last acceleration is brought about, although other similar accelerations are known to us. Thus hydrogen dioxide will slowly decompose in water. If ferric sulphate be added to the water, the decomposition is moderately accelerated. Cupric sulphate alone produces little if any effect upon the hydrogen dioxide, but if it be added to the mixture of hydrogen dioxide and ferric sulphate the reaction is enormously accelerated. Substances which act in this manner have been termed zymoexcitors. It seems probable, therefore, that the bile increases the ester-splitting action of the pancreatic juice by virtue of a zymoexcitor which it contains and that this zymoexcitor is in part, at least, lecithin.

[7] Bayliss and Starling: The Proteolytic Activities of the Pancreatic Juice. Jour. of Physiol., Vol. 30, p. 61.

[8] Berl. klin. Wochenschr., 1902, Nos. 38-39.

A CASE OF RIGHT-SIDED INFANTILE HEMIPLEGIA, WITH A DESCRIPTION OF THE PATHOLOGICAL CHANGES FOUND IN THE BRAIN AND THE SPINAL CORD.

BY ROBERT REULING, M. D., *Baltimore, Md.*

Although the literature of infantile cerebral palsies and their complicated symptomatology is voluminous and their pathology at the present time has at least a good working foundation, it is nevertheless surprising how comparatively few instances have been reported where the brain and spinal cord in these affections have been studied in their entirety. For this reason the following case is presented, inasmuch as a complete examination of the central nervous tissues was possible; unfortunately a clinical history and a satisfactory neurological examination were not obtained.

Sensory changes, however, are of rare occurrence in similar cases; in the present with exception of certain occasional pains in the affected members, a typical example of right-sided hemiplegia with marked contractures and osseous changes, due to its long standing (25 years), little was ascertained.

E. M., single, aged 28, white, born in the United States, was admitted to the lying-in wards of the University of Maryland Hospital in 1900. She complained of severe abdominal pains, and weakness. An abortion had been accomplished a few days preceding her entrance to the hospital. For the following notes and the use of the material I am much indebted to Drs. Alan and Stokes.

It was evident at the first examination that the patient had a septic infection. All means to combat this were tried; including irrigations. Her temperature ranged high and fairly regular for three days after admission, then became irregular, rigors were noted, and delirium of an unusually violent type soon set in. On the fifth day a soft systolic murmur appeared, best heard at the apex; the following day a very faint friction over the body of the heart suggested pericarditis. Soon a præsystolic murmur appeared, all pointing to a septic endocarditis. The abdomen was fairly distended and very sensitive in its lower quadrants.

The uterine discharge was ill-smelling and characteristic of septic endometritis. A few minute petechial hemorrhages appeared in the skin on the chest and abdomen. The urine throughout contained a considerable amount of albumen and casts; later some blood. She died on the tenth day after admission.

Clinical Notes.—Nothing is known as to her family history. When two years old she was taken ill with convulsions and on their cessation the right-sided paralysis was evident. Syphilis in later life could be fairly well excluded. She was immoral and had been the mother of one illegitimate child born at term. Epileptic convulsions have occurred from childhood, at what age they began is not known; they have been

less frequent since maturity. While in the hospital she had two severe general convulsions of an epileptic type, with frothy sputum. Her speech was considerably affected, a distinct hesitancy and lack of motor innervation was noted by all that saw her during the first days of her illness; as to the existence of a sensory aphasia this remains unproven. No athetoid movements were noted.

Autopsy.—Thirty hours after death. Body of moderately well nourished woman; little subcutaneous fat. Rigor mortis present. Abdomen moderately distended and highly tympanitic; skin over the same has a glossy appearance and the umbilicus is flattened. Faint bluish discoloration in left iliac region. Cornea in good condition and pupils regular. No external signs of advanced decomposition. A few petechial hemorrhages in lower chest and on the abdomen. A small linear scar over the right eye. Tongue very dry and covered with sordes, no scars found. No apparent facial asymmetry.

There is a striking difference in the appearance of the right and left upper extremities. The muscles of the right shoulder girdle and the entire right upper extremity are markedly wasted, the biceps muscle is practically a thick fibrous band, the humerus is also atrophied. The right arm is strongly flexed against the side of the chest and the forearm across it, the hand with its fingers flexed into the palm and indenting its surface, lies near the mid-body line over the xyphoid cartilage. Unless adhesions and muscle were torn the extremity could not be placed to the side of the body. An average difference of from 2.5 to 3 cm. is found in measuring the circumference of the right arm and forearm in comparison with the left extremity. The right lower extremity is also atrophied throughout, less markedly so than its upper fellow, it lies in a natural position, excepting that the foot is in a rigid, talipes equinus position, points sharply downwards while the toes are drawn dorsalwards. The tendo achillis was tense. The atrophy of muscle tissue seems most pronounced in the tibialis anticus and gastrocnemius. A shortening of 6 cm. in the right lower extremity was found and in approximating the two feet the toes of the right foot touched only the left internal malleolus.

On making the usual longitudinal incision a considerable amount of ill-smelling gas escapes from the abdominal cavity and on moving the intestines gurgling sounds are heard. An intense acute fibrino-purulent peritonitis, with occasional hemorrhages exists; the adhesions can be broken readily however. Pus is present between a few coils of the smaller intestines more being found in the pelvis where also a mucopurulent, slightly blood-stained fluid exists. The uterus is about the size of the organ at the 4th month of gestation, its muscle tissue is soft and friable. The perimetrium is injected. Uterine vessels are thrombosed, especially the veins. The pelvic glands are much enlarged. On section a raised patch about the size of a dollar is seen in the left half of the uterine endometrium, presenting a beautiful example of so-called diphtheritic inflammation. The kidneys show an acute parenchymatous nephritis and thrombi in many vessels. The liver is about normal size, and shows an acute parenchymatous necrosis. The spleen is moderately enlarged, very soft and vascular, the splenic corpuscles being obliterated. The heart shows its pericardial surface covered with a thin fibrino-purulent exudate the surface being still moist; the pericardial vessels are injected. A mass of thin, fresh adhesions attach almost the entire pericardial surface to the chest and lung pleura. A small amount of cloudy yellow fluid is in the sac. The heart is slightly dilated, its muscle is soft. On section a striking example of acute fibrinous exudate covers the leaflets of the mitral valve; this is raised above their surface and small fragments break off on handling the organ; the exudate extends slightly over to the endocardium and to the attachment of the papillary muscles. About the aortic valve a similar acute inflammation is in its incipiency. The lungs have a moderate pleuritic inflammation on the left side, especially near the cardiac region, also several patches of broncho-pneumonia and numerous emboli in the pulmonary vessels.

Description of the Brain.—On removing the calvarium, one is struck by the marked asymmetry of the two hemispheres; the left being much smaller than the right, this being true of the left hemisphere throughout. On removing the brain it is evident that the entire skull cavity is smaller than normal and the brain below the average size. The left anterior and middle fossæ of the skull are considerably smaller and more shallow than those on the right side, this being especially true of the middle fossæ. The posterior fossæ show, however, a reverse condition in that the right is smaller and more shallow than the left; the reason for this will be clear after considering the further examination of the brain. The dura mater over almost the entire left motor region was of a milky color, extending over the lower posterior central gyri and anterior occipital lobe. This membrane is much thickened and shows evidence of an increase in its vascular supply; in the region of the first, second, and third frontal convolutions a considerable retraction of the dura occurred amounting to the formation of a distinct cavity over the third frontal gyrus. When the removal of this cloudy portion of the dura was attempted, it proved intimately adherent to the brain surface.

Three small cysts were opened from which clear straw-colored fluid escaped, two in the first frontal and one in the second frontal regions. The dura and other membranes appeared about normal over the remaining brain surface. At the longitudinal fissure the left hemisphere showed a retraction of about 1.5 cm. below the level of the upper border of the right hemisphere while its anterior frontal tip was retracted an equal distance from its fellow on the right hemisphere. The only apparent change in the gross specimen of the cerebellum was an atrophy of the right hemisphere in its entirety, the left being normal. This atrophy was evident at first glance. There were no localized retractions of cerebellar tissue. The entire left half of the medulla showed a well-marked atrophy. The right half of the spinal cord below the decussation of the pyramidal tract was also atrophied. In the cord this atrophy was visible in the gross

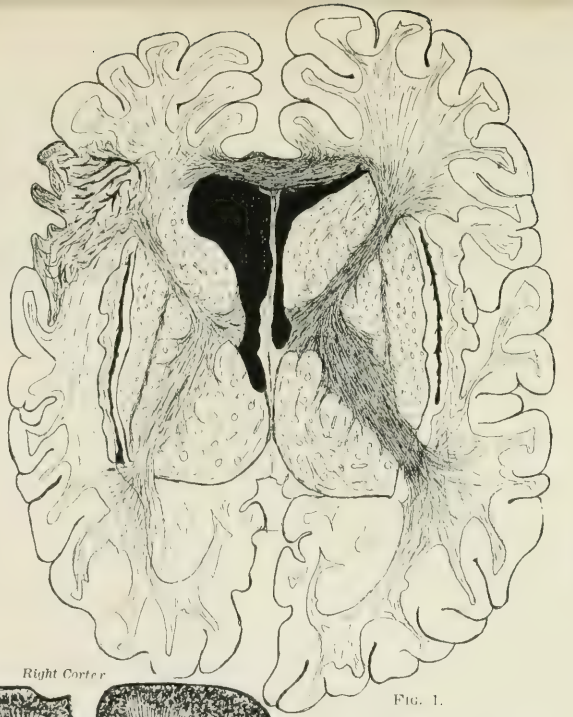


FIG. 1.

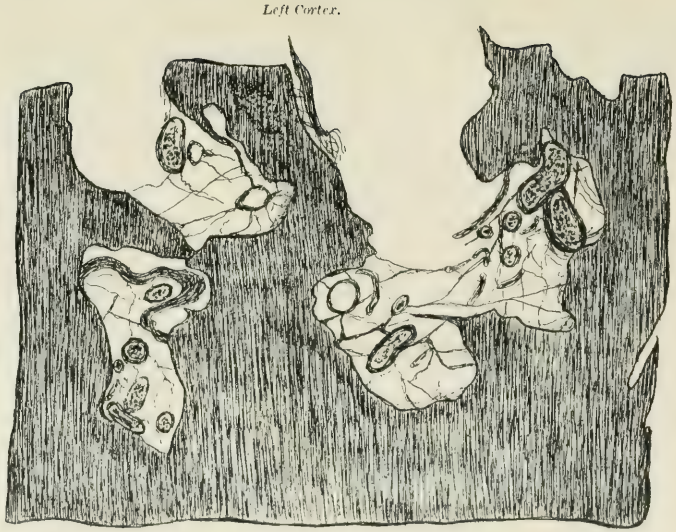


FIG. 3.



FIG. 2.

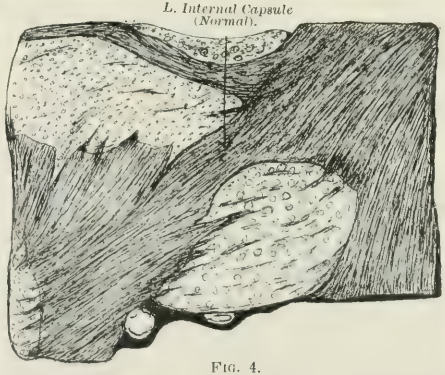


FIG. 4.



FIG. 5.

FIG. 8.

FIG. 9.

FIG. 6.

FIG. 7.

specimens as far down as the sacral region. The brain and sections of the spinal cord were placed in 10 per cent formalin.

The following is a description of the figures:

FIG. 1. This is a semi-diagrammatic drawing of a longitudinal section of the brain which passes through the lower second frontal region and includes the ventricles, the central nuclei as well as the internal and external capsules. For the more correct interpretation of the changes at the site of the lesions in the cortex and the changes in the capsular fibers and internal nuclei, sections stained by the Weigert-Pal method were used and the changes as seen under a dissecting microscope were added to the remaining entirely diagrammatic drawing.

One is immediately struck by the smaller dimensions and evident retraction of the entire left hemisphere. An almost total destruction of the tissue in the second frontal gyrus including the Island of Reil is found. A condition of a variable degree of microgyri is also evident in the cortex in the left frontal region. At the site of the lesion the blood vessels are increased and vessels of a larger size than are ever found in the normal gyri are found. The fibrous tissue infiltration is marked and its fibers rather coarse. The entire bundle of fibers making up the left internal capsule is about one-half the thickness of the right internal capsule. In the Weigert specimens by far the majority of the fibers of the left capsule stain only faintly, a few normal staining fibers being interspersed among them. The left lenticular caudate nuclei, especially the latter, are atrophied, also the left optic thalamus. The left lateral ventricle is moderately dilated.

FIG. 2. Weigert-Pal specimen of normal gyri taken from the right second frontal region, corresponding to the site of the lesion in the left frontal hemisphere.

FIG. 3. Weigert-Pal specimen with second Van Gieson staining. The section is from the site of the lesion in the second left frontal convolution. It shows a destruction of the greater portion of the gyrus; numerous cross-sections of blood vessels are seen, especially veins; coarse bands of connective tissue support these and replace to a certain extent the destroyed tissue. The formation of small cavities is seen, some lined by the dura, others by fibrous tissue. Considerable blood pigment is found on examining this specimen under the higher power and altogether there is no reasonable doubt but that a hemorrhage into the cortical substance was the cause of the pathological changes with formation of scar tissue and secondary atrophy of the pyramidal tract, internal nuclei and right hemisphere of the cerebellum.

FIG. 4. Weigert-Pal specimen from the region of the right internal capsule including portions of the optic thalamus, the lenticular and caudate nuclei. These appear normal and in marked contrast to the corresponding left region.

FIG. 5. Weigert-Pal specimen of the region of the left internal capsule including portions of the lenticular and caudate nuclei and optic thalamus. The atrophy of the internal capsule and optic thalamus is so evident in the drawing that further description is not needed. The oval and round clear spaces in the substance of the nuclei represent the enlarged perivascular spaces and lymph spaces about the nerve cells due to the retraction of the surrounding tissue.

FIG. 6. Represents the upper surface of the cerebellum. The well-marked atrophy of the right hemisphere is shown. This atrophy of the cerebellar hemisphere opposite to the side of the lesion has been described in several cases of cerebral infantile paralysis and it may be of interest to review briefly some of the opinions as to its cause. If we remember the existence of a fronto-cerebellar tract whose fibers pass from the motor region of one cerebral hemisphere to the cerebellar hemisphere of the opposite side, this change will be clear.

Gordinier gives the following description of this fronto-cerebellar tract. (Gordinier's Anatomy of the Central Nervous System, page 222.) "The fronto-cerebellar tract occupies rather more than the inner fifth of the crusta. The fibers of this tract come from the prefrontal lobe, and pass between the lenticular and caudate nuclei, occupying a large part of the anterior limb of the internal capsule, and a course downward on the inner side of the pyramidal tract, ending in the ventral portion of the pons Varolii; about the nerve cells of the nucleus pontis of each side are joined by fibers from the cortex of both cerebellar hemispheres, chiefly, however, with the cerebellar hemisphere of the opposite side. The fibers are the axones of the cells of Purkinje of the same and the opposite side, the latter fibers having crossed in the raphe, thus establishing a connection between the frontal lobe of the one side and both cerebellar hemispheres, but chiefly with the cerebellar hemisphere of the opposite side."

FIG. 7. Weigert-Pal section through the upper medulla showing the superficial and deep pontine fibers. As this section is above the decussation of the pyramidal tract, the degenerated fibers are found on the left side, in fact, the left half of the medulla is atrophied and even more so than represented in the drawing. The left pyramidal tract shows an advanced degeneration of its fibers so that few of them take up but a faint staining. The floor of the 4th ventricle is shallow and the nucleus of the hypoglossal nerves is seen close to the central raphe and just under the ventricular surface. In the deep pontine fibers of the left half of this section some atrophic changes are found.

FIG. 8. Weigert-Pal section through the medulla in the olivary region. In this section the atrophy of the left half of the medulla is still marked and more so than in figure 7. The left pyramidal tract is markedly atrophied and only a very few fibers stain at all. A few atrophic fibers are also seen in the lateral portion of the medulla above the large bundle of the pyramidal tract, these, no doubt, represent a subdivision of pyramidal bundles. The deep pontine fibers on the left side also show degenerative changes.

FIG. 9. Weigert-Pal section through the lower dorsal segment of the spinal cord. This shows a well marked degeneration of the right pyramidal tract as represented in the drawing by the lighter area in the postero-lateral portion of the cord. This area gradually shades into normal tissue and a narrow zone of normal fibers lies in the periphery of the cord, being fibers of ascending tracts. This degeneration in the crossed pyramidal tract on the right half of the cord can be traced to the lower sacral segment. Strange to say in none of the specimens from the medulla or spinal cord could a direct pyramidal tract be demonstrated and in reviewing the literature one finds that other observers have found it absent; no doubt, in such instances, all the motor fibers pass into the cord as a crossed tract. Sacki and Schmaus (Pathologie des Central Nervensystems, 1903, page 44), say: "We have previously mentioned the degenerative changes in the anterior direct pyramidal tract which lies on either side of the anterior sulcus of the cord. But this bundle does not at the present day hold the same importance it held in former years, in fact, it is at times impossible to demonstrate it in human beings." It is the best seen in lesions affecting the motor tract either in the internal capsule or crus cerebri or better still in those of the medulla or uppermost segments of the dorsal cord. Sacki and Schmaus also claim this tract has never been clearly demonstrated in lower animals. The following description of the anatomical relationships of the pyramidal tracts is taken from Gordinier's Anatomy of the Central Nervous System, page 91. "The motor fibers of the cord which are located in the direct and crossed pyramidal tracts arise from the motor areas of the brain, and represent the neuraxones of the large pyramidal cells, which are abundantly found in the third layer of the cortex. Their course from the cerebral cortex to the medulla will be described later. When they reach the medulla they occupy a large area on each side of the anterior median fissure, and at the first or second cervical nerves large bundles of fibers, or axones, representing about eighty per cent of the whole number, pass obliquely across to the opposite side, entering the posterior part of the lateral column of the cord, hence the name 'crossed pyramidal tract.' These crossed fibers become vertical and extend downward, gradually decreasing in size until they reach their termination at the level of the third or fourth sacral nerve, a small number of fibers continuing downward to terminate in the filum terminale. The neuraxones which do not cross representing about twenty per cent of the motor fibers, pass downward in the area of the cord adjacent to the anterior median fissure on the same side; hence they are called the direct or uncrossed pyramidal tract. They usually cease about the level of the mid-dorsal region. The motor neuraxones, like most of the long fibers of the columns of the cord, give off at different levels side branches or collaterals, which leave the parent stem at right angles. The axones, with the collaterals composing the crossed pyramidal tract of each side, pass forward and inward, entering the gray matter, where they break up about the motor nerve cells into innumerable fine filaments or aborizations. The neuraxones and collaterals of the direct pyramidal tract end, according to Lenhossek, in fine brush-like expansions about the motor nerve cells of the anterior horn of the same side. On the contrary, undoubted clinical and experimental evidence is at hand to prove that the greater portions of the fibers cross over through the anterior commissure to end about the motor nerve cells existing in the opposite anterior cornu. Most of the fibers of the direct pyramidal tract seem destined to the arm; hence the relation of the arm is almost exclusively with the opposite side. The fibers

of the tracts, direct and crossed, conduct impulses of voluntary motion from the motor areas of the brain to the muscles. If the fibers of the motor tract be destroyed by severing their connection with the cells of the motor area of the brain, there will result a motor paralysis of the opposite side of the body and a descending degeneration from the point of lesion throughout the entire extent of the tract. In the cord the degenerated areas will be the direct pyramidal tract of the same, and the crossed pyramidal tract of the opposite side. This degeneration is complete, involving the termination of the axones and collaterals, about the nerve cells of the anterior cornua, and is due to the loss of trophic or nutritional influence, which results from the severance of the nerve fibers from their mother cells, in the motor areas of the cortex. The peripheral portions of the tract on the contrary remain normal, because its nutrition is dependent upon the motor cells of the anterior cornu whose neuraxones form the peripheral portions of the tract." For a more complete discussion of the subject of infantile cerebral palsies, especially their relationship to the acute exanthemata and infectious diseases in general, the reader is referred to the article of Freud (Nothnagel's Specielle Pathologie und Therapie, Vol. IX, Part 3); that of Osler (Medical News, 1888, No. 2, 3, 4 and 5); Strümpell, Ueber die Acute Encephalitis der Kinder (Jahrbuch für Kinderheil Kunde, XXII, 1884); Strümpell on primary acute encephalitis (Deutsches Archiv für klin. Medicin, Vol. XLVII); also P. Marie, hemiplegie cérébrale infantile et Maladie infectieuses (Progrès méd., 5 Sept., 1885).

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NOTES ON NEW BOOKS.

New Methods of Treatment. By DR. J. LAUMONIER. Translated and edited from the second revised and enlarged French edition by H. W. SYERS, M. A., M. D. (*Chicago: W. T. Keener & Co., 1904.*)

This work treats in a general way of the recently introduced remedies. One cannot help wondering, on going over the book, whether the consideration of many of these is worthy of being kept in a permanent form. Of the large number of newer remedies described only a very few will be used by more conservative therapeutists. Considerable space is given to the discussion of various glandular extracts, but regarding these there is nothing specially new brought forward. The same may be said about the use of the various serums. One does not find anything of marked interest in this section, and under the heading "antityphoid inoculation," there is no mention whatever of the work of Wright. Notes regarding some of the newer drugs may be found useful, but one cannot help feeling that all that is valuable in this book might have been put in a quarter of the space. It is written in an agreeable style and the translation has been well done.

Medical Diagnosis. JOHN H. MUSSER, M. D. 5th edition. (*Lea Bros. & Co., 1904.*)

The early appearance of the fifth edition of Dr. Musser's book gives evidence of its extensive use in the profession. The present edition contains over one hundred more pages and one hundred and fifty-nine more illustrations than the last, making the book reach the upper limit of size practicable for a single volume.

The quality of the illustrations is variable, the wood-cuts being generally good, as are some of the colored plates, those picturing gross specimens, sputum, culture tubes, etc., being rather below the mark of excellence.

The general arrangement of the text has been maintained although some minor changes appear. Some chapters have been considerably expanded.

Among these, that treating of Internal Parasites has been rewritten and enlarged by the addition of some good cuts of parasites' eggs, etc. The subject is well brought up to date by the consideration of the newer parasitic forms such as *Uncinaria americana* and those of the trematode worms which have become of interest through our closer relations with the Far East.

The press work is good and the volume will prove acceptable to many students and practitioners who desire a general reference work on all phases of clinical diagnosis.

Appleton's Medical Dictionary. An illustrated dictionary of medicine and allied subjects in which are given the derivation, accentuation and definition of terms used throughout the entire field of medical science. Edited by FRANK P. FOSTER, M. D. (*New York and London: D. Appleton & Co., 1904.*)

If the present activity in the making of medical dictionaries continues, there seems little danger that the supply will not equal the demand. The volume before us of nearly 2000 pages seems more of a dictionary and less of an illustrated cyclopedia than almost any other upon the market. It represents conservatism in lexicography, and is prepared on strict lexicological lines. In the printing of words full weight is given to diphthongs; as, for example, œdema, œsophagus, hæmorrhage, and the like. The number of medical words given is very large and the book in fact, is somewhat cumbered with words, many obsolete terms being given. There is also a tendency to use unaccustomed words, often constructed on unimpeachable etymology in place of those which have become generally accepted; as, for example, *ecphyaditis* instead of *appendicitis*. The definitions are excellent and can be heartily praised. Certain definitions, however, are omitted; for instance, *dementia præcox* in the sense used by Kraepelin is not given, the nearest approach being the *acute dementia* of Pinel. The terms used by Ehrlich for example, to describe his side-chain theory of immunity, are many of them lacking, and one is compelled to conduct an elusive search through the dictionary and the supplement without getting after all any very clear idea as to their real meaning. Some of the newer terms of physiological chemistry are also lacking. The definitions of botanical terms are full and satisfactory.

The illustrations are not of a high order of merit, and the majority of them could have been omitted. The book itself is well and clearly printed. The volume as a whole is to be highly commended and its scope and execution remind one of the two first volumes of Foster's Encyclopedic Medical Dictionary which will always remain a monument to the learning and thoroughness of the editor.

Lectures to General Practitioners on the Diseases of the Stomach and Intestines. By BOARDMAN REED, M. D. Illustrated. (*New York: E. B. Treat & Co.*)

In his preface the author states that the majority of physicians now in practice have had no opportunity of learning the newer methods available in the diagnosis and treatment of diseases of the digestive system, and that books describing them are necessary. From this one might conclude that such books possibly do not exist. The writer, however, announces himself that books upon this subject have been multiplying during the last ten years, and that the subject has been treated most ably and exhaustively by several American writers, to say nothing of the works by foreign authors, which have been translated into English. Under the circumstances, it would therefore seem that the present work might have been dispensed with; but again the writer explains that there does not at present exist in the English language any work which in a single volume treats of the whole subject of diseases of the stomach and intestines from the standpoint of our present knowledge, and that the general practitioners and specialists in other lines desire such a work in a single volume. This, therefore, is the *raison d'être* of the author's work. It is written in the form of lectures, which are based in part upon those delivered to classes in the department of medicine of Temple College, Philadelphia, and in part upon his "Talks to General Practitioners" contributed by the writer to the International Medical Magazine, during the five years that the journal was under his editorial management.

Bearing in mind the standpoint from which the book is written, it may be considered a success, for it contains all those data, which the general practitioner is apt to look for in a work of this kind. It contains much therapeutic information, and considers besides questions of diet such resources as electrostatic currents and X-rays, the violet rays, the use of radium, mechanical vibration, manual therapy, hydrotherapy, exercise, etc.

In the accompanying prospectus of the publishers it is pointed out that in the writer's intercourse with chronic dyspeptic and nervous invalids, many of whom were exceedingly irritable and intolerant of all but the gentlest handling, the writer was led to devise methods as little unpleasant and disturbing as possible, compatible with accurate diagnosis and successful treatment. Such methods are to be found in the work before us.

A novel as well as useful feature is the introduction of a symptomatic guide to diagnosis, so far as the symptoms have to do with the gastro-intestinal apparatus.

As we have already suggested, the book will prove useful to the general practitioner for whom it is intended, but it is not a scientific work and often somewhat disappointing from this standpoint. Objectionable, and not in good taste is the ubiquitous and insistent appearance of the writer's Ego.

The publishers' work has been well done, so far as the text goes; the illustrations, however, which for the most part have been borrowed, are rather poor.

Essentials of Nervous Diseases and Insanity: their Symptoms and Treatment. By JOHN C. SHAW, M. D., late Clinical Professor of Diseases of the Mind and Nervous System, Long Island College Hospital Medical School. Fourth Edition. Thoroughly Revised. By SMITH ELY JELLIFFE, Ph. G., M. D., Clinical Assistant, Columbia University, Department of Neurology; Visiting Neurologist, City Hospital, New York, 12mo. Volume of 196 pages, fully illustrated. (*Philadelphia, New York, London: W. B. Saunders & Company, 1904.*)

This is a very creditable book which must be of great service to the medical student. The portion relating to the diagnosis of insanity is especially to be commended as it gives the student the latest views of an ever-shifting subject.

Essentials of Anatomy; including the Anatomy of the Viscera. By CHARLES B. NANCREDE, M. D., Professor of Surgery and Clinical Surgery in the University of Michigan, Ann Arbor. Seventh Edition. Thoroughly Revised. (*Philadelphia, New York, London: W. B. Saunders & Company, 1904.*)

In commenting on a previous edition we have had occasion to speak favorably of this students' manual. The present edition has been carefully revised and the anatomy of the nervous system has been especially considered. The book is designed expressly for students who are called upon to review their anatomy.

A Compend of Medical Latin Designed Expressly for Elementary Training of Medical Students. By M. T. ST. CLAIR, A. M., Professor of the Latin Language, etc. Second edition, revised. (*Philadelphia: P. Blakiston's Son & Co., 1904.*)

This is a clearly written and practical little compend of medical Latin prepared expressly for those who have entered upon the study of medicine without a previous knowledge of the language. At best the knowledge which can be acquired even from the best compend of this character is a make-shift and not in the line of thoroughness. If a student must secure a modicum of Latin and is satisfied with it, we know of no short treatise which will prove as useful as the one under review. The list of abbreviations is full and the vocabulary is good.

BOOKS RECEIVED.

State Board of Health of the State of Ohio. Seventeenth Annual Report. For the year ending December 31, 1902. 8vo. 508 pages. 1904. Springfield, Ohio.

A Text-Book of Human Physiology. By Albert P. Brubaker, A. M., M. D. With colored plates and 354 illustrations. 1904. 8vo. 699 pages. P. Blakiston's Son & Co., Philadelphia.

Appleton's Medical Dictionary. An Illustrated Dictionary of Medicine and Allied Subjects, in which are given the Derivation, Accentuation and Definition of Terms Used Throughout the Entire Field of Medical Science. Edited by Frank P. Foster, M. D. 1904. 4to. 1991 pages. D. Appleton and Company, New York and London.

A System of Practical Surgery. By Prof. E. von Bergmann, M. D., Prof. P. von Bruns, M. D., and Prof. J. von Mikulicz, M. D. Volume IV. Translated and edited by William T. Bull, M. D., Edward Milton Foote, M. D., Carleton P. Flint, M. D., and Walton Martin, M. D. *Surgery of the Alimentary Tract.* 1904. 8vo. 755 pages. Lea Brothers & Co., New York and Philadelphia.

The Principles and Practice of Gynecology. For Students and Practitioners. By E. C. Dudley, A. M., M. D. Fourth edition, revised. With 419 illustrations in colors and monochrome, of which 18 are full-page plates. 1904. 8vo. 771 pages. Lea Brothers & Co., Philadelphia and New York.

Saunders' Question-Compends, No. 21. Essentials of Nervous Diseases and Insanity. Their Symptoms and Treatment. By John C. Shaw, M.D. Fourth edition thoroughly revised by Smith Ely Jelliffe, M. D., Ph. D. Illustrated. 1904. 12mo. 196 pages. W. B. Saunders & Co., Philadelphia, New York, London.

Saunders' Question-Compends, No. 7. Essentials of Materia Medica, Therapeutics and Prescription Writing. Arranged in the form of questions and answers. Prepared especially for students of medicine. By Henry Morris, M. D. Sixth edition, thoroughly revised by W. A. Bastedo, Ph. G., M. D. 1904. 12mo. 294 pages. W. B. Saunders & Co., Philadelphia, New York, London.

Saunders' Question Compends, No. 3. Essentials of Anatomy. Including the Anatomy of the Viscera. Arranged in the form of questions and answers. Prepared especially for students of medicine. By Charles B. Nancrede, M. D. Seventh edition, thoroughly revised. 1904. 12mo. 419 pages. W. B. Saunders & Co., Philadelphia, New York, London.

Clinical Lectures on Mental Diseases. By T. S. Clouston, M. D., Edin., F. R. C. P. E. Sixth edition. 1904. 12mo. 738 pages. Lea Brothers & Co., Philadelphia and New York.

Physician versus Bacteriologist. By Prof. Dr. O. Rosenbach, of Berlin. Authorized translation from the German by Dr. Achilles Rose. 1904. 12mo. 462 pages. Funk and Wagnalls Company, New York and London.

Hand-Book of the Anatomy and Diseases of the Eye and Ear. By D. B. St. John Roosa, M. D., LL. D., and A. Edward Davis, A. M., M. D. 1904. 16mo.. 297 pages. F. A. Davis Company, Philadelphia.

Arteria Uterina Ovarica. The Utero-Ovarian Artery, or The Genital Vascular Circle. Anatomy and Physiology, with their Application in Diagnosis and Surgical Intervention. By Byron Robinson, B. S., M. D. 1903. 4to. 182 pages. E. H. Colegrove, Chicago, Illinois.

Refraction and How to Refract. Including Sections on Optics, Retinoscopy, the Fitting of Spectacles and Eye-Glasses, etc. Third edition. Two hundred and fifteen illustrations, thirteen of which are colored. 1904. 8vo. 314 pages. P. Blakiston's Son & Co., Philadelphia.

A System of Practical Surgery. By Prof. E. von Bergmann, M. D., Prof. P. von Bruns, M. D., and Prof. J. von Mikulicz, M. D. *Volume V. Surgery of the Pelvis and the Genito-Urinary Organs.* Translated and edited by William T. Bull, M. D., and Edward Milton Foote, M. D. 1904. 8vo. 789 pages. Lea Brothers & Co., New York and Philadelphia.

Practical Dietetics. With Reference to Diet in Disease. By Alida Frances Pattee. Second edition, revised and enlarged. 1904. 12mo. 311 pages. Published by the Author, New York City.

A Treatise on Obstetrics. For Students and Practitioners. By Edward P. Davis, A. M., M. D. Second edition. Illustrated with 274 engravings and 39 plates in colors and monochrome. 1904. 8vo. 809 pages. Lea Brothers & Co., Philadelphia and New York.

A Practical Treatise on Diseases of the Skin. For the Use of Students and Practitioners. By James Nevins Hyde, A. M., M. D., and Frank Hugh Montgomery, M. D. Seventh and revised edition. Illustrated with 107 engravings and 34 plates in colors and monochrome. 1904. 8vo. 938 pages. Lea Brothers & Co., Philadelphia and New York.

Diseases of the Nose, Throat and Ear, and their Accessory Cavities. By Seth Scott Bishop, M. D., D. C. L., LL. D. Third edition, thoroughly revised and enlarged. Illustrated with ninety-four colored lithographs and two hundred and thirty additional illustrations. 1904. 8vo. 564 pages. F. A. Davis Company, Philadelphia.

A Practical Treatise on Genito-Urinary and Venereal Diseases and Syphilis. By Robert W. Taylor, A. M., M. D. Third edition, thoroughly revised. With 163 illustrations and 39 plates in colors and monochrome. 1904. 8vo. 757 pages. Lea Brothers & Co., New York and Philadelphia.

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Beauty Through Hygiene. Common Sense Ways to Health for Girls. By Emma E. Walker, M. D. Illustrated. 1904. 16mo. 306 pages. A. S. Barnes & Company, New York.

How to Cook for the Sick and Convalescent. Arranged for the Physician, Trained Nurse, and Home Use. By Helena V. Sachse. Second edition, revised and enlarged. 1904. 12mo. 297 pages. J. B. Lippincott Company, Philadelphia.

International Clinics. A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles on Treatment, Medicine, Surgery, Neurology, Pediatrics, Obstetrics, Gynecology, etc. Edited by A. O. J. Kelly, A. M., M. D. Volume III. Fourteenth Series, 1904. 8vo. 302 pages. J. B. Lippincott Company, Philadelphia.

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Progressive Medicine. A Quarterly Digest of Advances, Discoveries and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M. D., assisted by H. R. M. Landis, M. D. Volume III. September, 1904. 8vo. 284 pages. Lea Brothers & Co., Philadelphia and New York.

Essentials of Bacteriology. Being a Concise and Systematic Introduction to the Study of Micro-Organisms. By M. V. Ball, M. D. Fifth edition, thoroughly revised by Karl M. Vogel, M. D. With ninety-six illustrations, some in colors, and six plates. 1904. 12mo. 243 pages. W. B. Saunders & Company, Philadelphia, New York, London.

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A Compend of Medical Latin. Designed Expressly for Elementary Training of Medical Students. By W. T. St. Clair, A. M. Second edition, revised. 1904. 12mo. 131 pages. P. Blakiston's Son & Co., Philadelphia.

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Surgical Emergencies. The Surgery of the Abdomen. Part I. Appendicitis, and Other Diseases about the Appendix. By Bayard Holmes, B. S., M. D. 1904. 12mo. 350 pages. D. Appleton & Company, New York.

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A Treatise on Bright's Disease and Diabetes. With Especial Reference to Pathology and Therapeutics. By James Tyson, M. D. Second edition. Illustrated. Including a section on the Ocular Changes in Bright's Disease and in Diabetes. By George E. de Schweinitz, M. D. 1904. 8vo. 381 pages. P. Blakiston's Son & Co., Philadelphia.

Multiple Personality. An Experimental Investigation into the Nature of Human Individuality. By Boris Sidis, M. A., Ph. D. (Harvard), and Simon P. Goodhart, Ph. B. (Yale), M. D. 1905. 8vo. 462 pages. D. Appleton and Company, New York.

Medical Laboratory Methods and Tests. By Herbert French. 1904. 16mo. 152 pages. W. T. Keener & Co., Chicago.

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CONTENTS.

PAGE

On the Teaching of Anatomy as Illustrated by Professor Barker's Manual. By Franklin P. Mall, ... 29

The Anatomical Laboratory of the University of California. By Joseph Marshall Flint, M. D., ... 32

Anatomical Material—its Collection and its Preservation at the Johns Hopkins Anatomical Laboratory. By Franklin P. Mall, ... 38

The Development of Grave Robbing in England. By G. Canby Robinson, M. D., ... 42

On Flechsig's Investigations on the Brain. By Florence R. Sabin, M. D., ... 45

A Note on the Developmental Relations of the Kidney and Ureter in Human Embryos. By Augustus G. Pohlman, M. D., . . 49

Abnormalities in the Form of the Kidney and Ureter Dependent on the Development of the Renal Bud. By Augustus G. Pohlman, M. D., ... 51

PAGE

On the First Appearance of the Renal Artery, and the Relative Development of the Kidneys and Wolffian Bodies in Pig Embryos. By Eben C. Hill, ... 60

High Bifurcation of the Brachial Artery with Reunion at the Elbow. By Minerva Herrinton, ... 65

Fixation of Tissues by Injection into the Arteries. By Burton D. Myers, M. D., ... 66

A Convenient Still to Make Absolute Alcohol. By William J. Calvert, M. D. 68

Announcement Concerning Graduate Instruction in the Medical Department of the Johns Hopkins University. By W. H. Howell, M. D., ... 70

Summaries or Titles of Papers by Members of the Hospital or Medical School Staff appearing Elsewhere than in the Bulletin, 73

ON THE TEACHING OF ANATOMY AS ILLUSTRATED BY PROFESSOR BARKER'S MANUAL.[1]

By Franklin P. Mall.

Professor Barker has given us a profound work upon the nervous system and an excellent English edition of Spalteholz's superb Atlas of Human Anatomy. To these he now adds a laboratory manual of anatomy, one of the best dissecting-room guides which has ever been published.

With the exception of those in a few medical schools the dissecting-room is a pretty poor specimen of a laboratory, due mainly to the lack of competent instructors. The course is generally "go as you please," and in order to accomplish anything it requires students of ability and earnestness with a power to plan ahead, and for them Barker's Manual will be a great aid. From it they will receive guidance, which otherwise could be received only from competent teachers. The Introduction to the Manual points out to the student the well-known methods for unraveling the human body, by which they obtain knowledge at first hand. "Careful practical work in the dissecting-room is the only means a medical student has of obtaining an independent view of the gross structures of which the body is composed. He should learn to *see* what comes under his eye. He should try by his own independent activity to see all that is there, for the student who learns to see only what he is told to see, or what is pointed out to him, will be spoiled for the study and the practice of medicine." Professor Barker seems to ignore wholly that anatomy (?) which consists of memory feats brought about by drill masters who have prepared the student for no one knows what. "The very first dissection," he says, "may be all-important as regards the subsequent dissections. He who fails in his earliest dissection to acquire the habit of working according to a definite method, seldom learns later to become an exact, quick, and careful dissector. It is almost hopeless to try to make a

[1] A Laboratory Manual of Human Anatomy. By Lewellys F. Barker, M. B., Tor., Professor and Head of the Department of Anatomy, in the University of Chicago and Rush Medical College. Assisted by Dean De Witt Lewis, A. B., M. D., and Daniel Graisberry Revell, A. B., M.B., Instructors in Anatomy in the University of Chicago. 8vo. 583 pages and 298 illustrations, many in colors. (Philadelphia: J. B. Lippincott Company, 1904).

man do exact and clean work in the dissecting-room after he has once formed inaccurate and dirty habits.... If a dissector permit himself to expose structures roughly, to isolate them incompletely, and to clean them imperfectly, so that his dissection becomes indistinct, bad-smelling, and repulsive-looking, he will quickly lose interest in his work, slice the part desperately, neglect it, stay away from it, and fail utterly to benefit by it. . . . The thorough dissector is much more likely to become a fine discriminating physician and an effective, progressive surgeon." Not one word do we read in this excellent book about memorizing names, systems of mnemonics, quiz-classes and final examinations. Nowhere do we read that the 5000 questions which were placed before me while a medical student gives the "royal road" to knowledge.

The book is written as a guide to earnest students who, with the aid of good teachers, desire to dissect the human body and thereby obtain a conception of it. If a student wishes to study anatomy he is most successful when he obtains his knowledge through actual experience in the dissecting-room, and to do this he must learn to unravel the structures of the body, and to see, classify and describe what he has done. While working thus he is naturally led into the literature of the subject which, when drawn upon later in life, should enable his imagination to see the part described in three dimensions of space.

The methods of isolating the structures of the human body have been well established, and certain rules for dissection have been formulated. These rules are well known to anatomists, and it is best for the students when they are taught them by the most experienced teachers. To do this the teachers must accompany the students in their daily work, and unless this is the case the ship will run upon the rocks, even if the nautical almanac and the quadrant are in the hands of the sailors. It is the ideal of the instructor, the word here and the word there, that means so much to the student. The great bulk of the time of the student is to be occupied by his own work—dissecting, reading, drawing, comparing and reflecting—and here the Manual may help out immensely. In it the thousand and one hints are given, and questions are answered in order, as in a dictionary. Professor Barker has written what the teacher says many times, and I shall be much gratified if, in future, it saves me some words.

In arranging the material, Barker has followed closely the order given in Cunningham's Manual, thus enabling the student to use both books at the same time. The steps and technique are to be gotten from Cunningham, while the hints and directions for study are found in Barker's Manual.

It is possible to classify the teaching of anatomy in America under four heads.

The first and lowest order is found in those schools which give a course of crude lectures on anatomy with a dissecting-room in which the work is not directed, but is done in a superficial way. Often the students do not dissect at all. At best they use a brief guide or a quiz compend which enables the students to "learn enough" to pass the examinations. Barker's Manual will be of no use—will be wholly lost—to both students and professors in medical schools which conduct their course in anatomy in this way.

The teaching of anatomy is of a higher order when it follows closely some text-book, especially Gray, when it has lectures and recitations and enough work in the dissecting-room to enable the students to identify the grosser structures, thereby giving enough information to enable the students to pass State examinations. Most of the medical students desire courses of this order. Barker's Manual will be of little value to them, but it is to be highly recommended to their teachers, for through them it will do the greatest good.

In a third and higher order of medical school, about twenty of which may be counted, the course is given to aid the students in their subsequent medical studies. Practical things are pointed out in lectures, and emphasized again in the dissecting-room, and finally the student is examined upon them. Both students and teachers work pretty hard, and at the end of the course all feel that much good has been done.

A professor told me recently that he made his course "truly practical" by teaching only the essentials which he learned, by canvassing all of the clinical teachers. What they considered essential was taught, and what was considered unessential was excluded from the course. This practical knowledge he drilled into his students by means of lectures, quizzes, and thorough work in the dissecting room, and the results were most satisfactory to all concerned. To him and to his better students I most cordially recommend Barker's Manual. It will give them something to think about, and by that very effort will do them much good.

In the fourth order of anatomical course it is considered that there are others to be satisfied besides the teachers in a few practical branches,—there are the teachers in the other sciences, physiology, neurology, pathology, as well as anatomy itself. A student told me recently that he had been studying one thing to help him in another all of his life, and he was dead tired of it; he now desired to study things that were worth studying for their own sake. For him anatomy could not be considered an ancillary science. In presenting a science to students no attitude can be defended, except that in which the science is studied for its own sake. In so doing the development of the student cannot possibly be ignored, for understanding and self-development go hand in hand.

"Many students in the past have entered the dissecting-room with an utter lack of independent power of observation, of examination and of description, and yet these three qualities are absolutely necessary for the man who is to engage successfully in the practice of medicine. While it is to be hoped that the advance in the requirements for admission to professional schools, leading as it does to observational work in physics, chemistry and biology preliminary to the work of the medical course, will bring the students to our laboratories of anatomy better prepared than hitherto for the independent observation of anatomical structures, there can still be but little doubt that many students will learn how really to study and observe first in the dissecting-room. How important it is that the habits formed at this early period of the profes-

sional course should be such as will be of value to the student later, such as he would desire to have throughout his professional career! If he have learned to be exact and steady, systematic and thorough, cleanly and artistic in his work in the dissecting-room, how much better for him than if at the outset of his career he become satisfied with superficial observation, with interrupted and irregular activity, with disorder and uncleanliness! The habits formed in the anatomy building have their effect upon the whole life of the physician. The student in the beginning should aim not so much at rapidity as at method. When he has once formed the habit of proceeding always according to a careful method, the rapidity will quickly follow.

"It is sometimes asked: 'Why should the medical student spend so much time and take so much pains in making a careful and beautiful dissection? Is it not time wasted to work out the smaller branches of the nerves and blood-vessels?' Experienced teachers who require thorough work are not disturbed by such inquiries. Those who have had the best opportunity for judging assert that it is only when a man succeeds in making a fine dissection that he gains an interest and pleasure in an occupation, which may not at first be attractive to him. Further, the impotance of working out the finer structures lies not always so much in the actual knowledge of these structures gained by the student, as in the acquisition of the habit of thoroughness of observation and investigation. The medical student who in the dissecting-room dissects out only the main trunks of the vessels and nerves, or only the structures which, at the moment, seem to physicians and surgeons of greatest practical import, is likely, as a clinician, to be satisfied with the detection of the more obvious and superficial symptoms, to the overlooking of the less prominent symptoms and the more obscure physical signs."

It is especially for students and teachers of anatomy in the best medical schools that Barker's Manual will be of great value.

It is generally admitted that the most valuable training in anatomy is obtained in the dissecting-room, and it is in this place where the best teaching can be done. The instructor, text-books and manuals are only aids to be used as guides. The main effort must be on the part of the student, for it is he who is to obtain the knowledge through his senses. He must unravel the structures, arrange and classify them, reflect over them and express them, best by means of drawings, in order to get the most out of his work. His work is easy in proportion to his power to see in three dimensions of space, and to aid this models and pictures are to be used. It happens, also, that anatomy has an extensive language of its own and he must acquire some of this in order to express his knowledge of the subject in words, as well as to gain command of its extensive literature. While a few will excel, every student must be able to do this in part at least, before he is proficient in anatomy.

It is relatively easy to dissect the human body successfully, and when a student can attach names to the structures he has dissected he is usually satisfied. The second step, studying the part is the difficult one, one that is mastered by but few students. The movement in anatomy in America during the past twenty years has been to make the study inductive, just as Huxley would have it, and in order to bring this about students have been introduced to anatomy in the dissecting-room rather than in the lecture-room. My own experience is that nearly all students can be made good dissectors in less than a week, and many of them in a day, but it takes a number of weeks before they are able to get the full benefit of their own dissections. If, with pictures to aid the imagination, they can look ahead and if, with pencil they draw what they have dissected, they have accomplished much for they work independently. Such students the instructor can aid with advice, he can discuss next steps with them, he can aid them in reading and in drawing, all of which he does with the greatest of pleasure. But many students do not have this gift and to teach them is difficult. Barker's Manual not only helps them, but does not retard the talented students. Superficial students can never use it as a quiz-compend, nor can it be memorized. In the description of the back, for example, Barker says on page 45:

"Reflect the two triangular flaps of skin, taking none of the fat of the superficial fascia with it. Have your atlases open before you. Having ascertained the region in which the medial set of cutaneous vessels and nerves is likely to be found, with the knife make a small cut through the superficial fascia down to the deep fascia. With the special heavy probe recommended, separate an area of the superficial fascia until you encounter the trunk of a blood-vessel or a nerve coming through the deep fascia from below to enter the superficial fascia. It is common to find a nerve, an artery and a vein together. Carefully separate the structure or structures found from the superficial fascia, tracing the blood-vessel or nerve as far as possible and cleaning it thoroughly. In this way, isolate all the superficial blood-vessels and nerves in the medial and lateral areas in which they occur. The nerves and blood-vessels will be found emerging through the deep fascia. Their course and ramifications in the superficial fascia are to be traced out without removing the fat or disturbing the relations of the structures any more than is necessary in exposing them. It should be borne in mind that it is only the natural relations that are of importance, and not the artificial relations due to dissection. Hence, each structure should be studied as it is worked out, instead of its study being deferred until after it is isolated and cleaned. When the cutaneous nerves and vessels and superficial glands have been thus exposed, a drawing of these should be made; or the drawing may be made concurrently with the dissection, being then an aid to the determination of the exact relations.

"The deep fascia should be cleaned (by careful removal of the superficial fascia by blunt dissection) and its extent, nature and attachments studied. The fasciæ should then be removed piece-meal. In cleaning the surface of the muscles, place the body in such a position that the muscle-fibers will be rendered tense and carry the knife in the direction which

permits removal of the fascia with the least disturbance of the underlying muscle. Care should be taken to avoid giving a ragged appearance to the surface of the muscle. As soon as the trunk of a nerve or blood-vessel is found, ascertain its name from a study of the illustration in your atlas. Look up this name in the index to your Systematic Human Anatomy and refer to the author's description. When handling a nerve, blood-vessel or indeed any structure, form the habit of repeating to yourself its name; this practice is extremely helpful in fixing the association between the structure and the name which is the sign for it. Also, when reading, write down every new term met with and learn its meaning, both literal or etymological and applied or derived."

After this there follows a list of nerves, arteries, veins and muscles in the order of their appearance, with reference to figures in the Manual as well as in Spalteholz's Atlas and other books. The subject is presented just as if the reader really wanted to study anatomy. It is illustrated with 298 figures, in great part taken from Toldt's Atlas, and from Poirier and Charpy's Anatomy.

Throughout the Manual the new nomenclature is used with the old names, when they differ much, placed in brackets. Both English and Latin terms are given. In my opinion, it would be better if only the anglicized new nomenclature were given, much as has been done in Cunningham's Anatomy. The international terms (Latin) can be found easily by referring to Spalteholz, which is to be used in connection with this Manual. However, it is very desirable that the new nomenclature should be used, for then the student commands a language of anatomy which is not only English but is also international.

The names in anatomy were introduced by many authors during past centuries, which naturally led to the formation of numerous synonyms. Over a century ago this chaotic condition was deplored by Sömmering (Bau des menschl. Körpers, S. XII, 1800), who then suggested that anatomists construct a uniform nomenclature as the botanists had done. But each new attempt brought only a new set of synonyms, for there was no Linnaeus in anatomy who could do the work. The numerous names then, as at present, made the study of anatomy very much more difficult than it would be were the terminology simple and rational. At that time, Dumas (1797) attempted to make it rational, however, without success, as is the case with Wilder's nomenclature in recent years. A great authority, as a congress, was necessary to bring about this reform. Henle (Anatomie, S. VII, 1858) revised the list of names very markedly, placing the synonyms in foot-notes, not using them indiscriminately as pedants love to do. His reform did much good and also caused much confusion; we have to thank him, however, for the terms, dorsal, ventral, sagittal, frontal, medial and lateral. Later, Owen added to them the terms, distal and proximal.

Finally, the suggestion of Hyrtl (Anatomie, S. 35) bore fruit. He proposed that the Naturforscher Gesellschaft, from which the Anatomische Gesellschaft sprang, take up the subject and give the nomenclature of anatomy a thorough scientific and philological revision. This was finally done, under the leadership of His. The international committee, with Sir William Turner, Cunningham and Thane to represent England, supported by the Academies of Berlin, Munich, Vienna, Leipsic and Buda-pest, and the Anatomische Gesellschaft, after six years of hard work, finally rendered a satisfactory report (see His, Nomina Anatomica, 1875), which has been accepted generally by the anatomists of the world. In our language we have a number of comparative anatomies, two very important atlases (Spalteholz and Toldt), a text-book (Cunningham, in part), and now Barker's Manual which uses this terminology. Students, physicians and some professors think something radical has been done, and fear that if they accept it they must unlearn something,—they know not what,—but when they realize that it is the Italian, the German, the Swede and others must change their terminology much more than the Englishman, they will welcome the new language. It differs less from our terminology than from that in any other language. The His nomenclature (BNA) has reduced the 30,000 anatomical terms to 5000, and of them 4500 are the same as the English terms. Of the 500 terms which differ from the old, the change is usually slight. Nearly all of the radical changes were made in the neural terms, and in general these have been accepted by all writers. Had Barker anglicized the names of BNA, but few readers of the Manual would notice that he has used the new nomenclature.

It is to be hoped, in the interest of anatomy and scientific medicine, that Barker's Manual will receive a wide circulation.

THE ANATOMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA.

By Joseph Marshall Flint, M. D.

In the past few decades many papers have been published upon the ends and aims of anatomy, as well as upon its pedagogical methods and the construction of laboratories in which it is taught. These articles cover this field thoroughly and well. It seems, therefore, quite unnecessary to make another contribution to this, already, large literature. Hitherto, most of the larger anatomical institutes have been constructed anew where the director has had an opportunity to express his ideas entirely unhampered by already existing structures. As it is sometimes necessary, however, to reconstruct or readapt buildings already in existence for the use of an anatomical department, our experience in the University of California may have some new interest and possibly some practical bearing. Here, it was essential to rearrange the quarters in a

building, planned for the medicine in vogue before the extensive introduction of the laboratory system. It may be well to state, however, that these rooms lent themselves admirably to our needs. It is, indeed, probable that most quarters supplied with adequate space and light could be transformed into a serviceable laboratory adapted to the needs of modern anatomy. In the rearrangement of the space at our command, attention was paid to the following objects: First, the necessities of teaching and, secondly, facilities for research. Under these two heads and their ramifications, all the needs of anatomy may be supplied. It was deemed wise to provide space and equipment for a class of 50 students, although our maximum attendance in any one class has thus far been but 42.

Naturally, in anatomy, as in other educational branches, the chief essentials of equipment are men and not rooms nor microscopes. In this country, for some reason, it has been difficult to preserve a proper ratio between staff work and equipment. In some institutions splendid equipments are insufficiently manned, while in others it is often true that good men are handicapped either by a lack of materials with which to do their work or else are overburdened with excessive routine. Perhaps we are in what one college president terms "The Stone Age," in which our university resources are too apt to crystallize into bricks and mortar instead of contributions to the various fields of science. According to A. G. Mayer's[1] recent study on the material and intellectual development of American universities, things have not improved much in the last decade; but in the case of the medical branches of university life, there has been a noticeable exception. In recent years, particularly in the so-called scientific branches of medicine, several well-equipped and well-manned laboratories have been established. Indeed, there seems to be a general tendency to conduct the first two years of medicine at least upon a university basis. This means, in addition to routine teaching, a portion of the energy of the department must be spent in productive scholarship. In the University of California members of the anatomical staff are expected to devote one-half of their time to research.

The building, in which the Medical Department of the University of California is sheltered, was constructed for the University by the State of California, in 1898. It consists of a substantial three-story building, constructed of granite and buff brick, situated on Parnassus heights and commanding a magnificent view of the Pacific Ocean and the bay of San Francisco. The old quarters allotted to anatomy were on the top floor, where one large dissecting-room with roof light and a few smaller rooms were allotted to the students in anatomy. Additional space on the lower floors was obtained for an histological laboratory, store-rooms, and photographic-room. Adequate room in the basement for the embalming and preservation of anatomical material was arranged in the first plan of the building.

[1] Material versus Intellectual Development of our Universities. Science, Vol. XX, 1904.

Dissecting-Rooms.

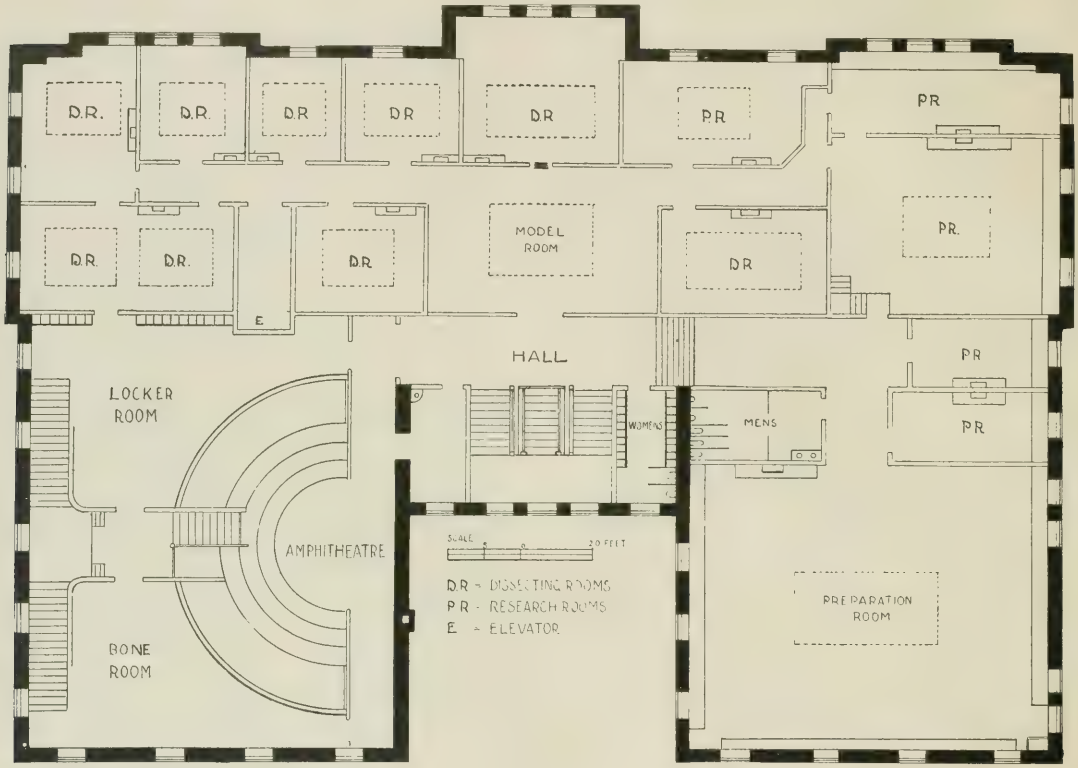
The large dissecting-room was provided with roof light, a tarred floor and rough brick walls. In the conversion of this space to more modern dissecting-rooms several points concerning anatomy in this country had to be borne in mind. In the first place, anatomical material was often poorly preserved and frequently scant in quantity; in the second, by tradition, students who crossed the threshold of a dissecting-room assumed at times that they were absolved from all standards of good conduct. Hats were worn; students dressed in outlandish costumes. Smoking was generally permitted, and boisterous conduct, accompanied by the throwing of material were not infrequent occurrences. To break this tradition and to obtain in a measure the morale and seriousness characteristic of the students in other departments of the university, we profited by the experience of Professor Mall of the Johns Hopkins University, who, in the construction of his laboratory, went on the assumption that students should be divided into small groups and should be provided with dissecting-rooms, which resemble a modern laboratory more than they do a stable. Accordingly, the large dissecting-room was re-covered with a new floor, and was cut up into a series of small rooms, each, with a capacity of from 1 to 4 tables, thus segregating small groups of students. In this way fewer distractions occur and one obviates the inevitable noise that occurs when even larger bodies of well-behaved students are quartered in the same laboratory. The rooms, moreover, were fitted with especial care to make them clean, neat, and attractive, hoping in this way to obtain the effect of a pleasant environment upon the work of the students during the periods of dissection. The large room was 35 by 110 feet, and was subdivided into eight small dissecting-rooms, a research room and a museum. The largest of these small dissecting-rooms is 20 by 21 feet, with a comfortable capacity of four tables and a maximum of six, while the smallest is 12½ by 15 feet, and holds one dissecting table conveniently. The remainder are so arranged as to hold from one to three tables. The rooms are provided with heavy tables with zinc tops, draining toward the center into a bucket suspended beneath the table. Adjustable arm-rests and book-stands also form part of the equipment. As soon as the body is cut in parts, students are no longer forced to work together, and in consequence one or two small tables with book-stands are provided in each dissecting-room. There is a sink with running-water and a large drip-board to hold parts while they are being moistened, or for the study of the viscera. Each room has, besides, an articulated skeleton for convenient reference and a blackboard upon which schemata may be drawn and relations studied. During the period of dissection the student is held responsible for his material, which must be carefully wrapped in cheesecloth at the close of each laboratory period. These wrappings are moistened in a solution of carbolic acid, glycerine and water, made according to the following formula:

Water	1000 cc.
Glycerine	30 cc.
Carbolic Acid	20 cc.

This procedure prevents desiccation and, at the same time, acts to a certain extent as a preservative.

The Museum.

No space was available for use as a museum and, accordingly, the entrance hall to the dissecting-rooms was left large for this purpose. Its dimensions are 20 by 32 feet and it contains sixteen unit museum cases for the exhibition and storage of models that are used either for demonstration or teaching purposes. Here also are kept the most interesting variations which have been found from time to time in the dissecting-rooms, as well as examples of research work which has been done by students and members of the teaching staff. The latter are valuable for the purpose of demonstration, and often act as a stimulus for more serious students to engage in research work. The location of the museum in this hall, which was forced upon us by lack of space in other parts of the building, has proved most fortunate. In the experience of most laboratory workers, students in the attendance upon regular courses very rarely avail themselves of the opportunities afforded by a museum. The interest in such specimens is not sufficient to overcome the inertia of any but the best students. But if exhibition cases are so placed that they must be passed in going to and from the regular work, specimens are frequently studied when, under ordinary circumstances, they would not be seen. In the course of a year's work, students register many thousands of visual impressions simply in passing back and forth. The museum is provided with two large unit tables for the study of its preparations, but these are naturally exposed to the noise caused by students in transit. Were I to build a laboratory anew, I should consider as one of its most important features the placing of the museum in the main thoroughfare of the laboratory. At the same time it would be advisable to have at one side an exhibition room where specimens could be studied in quiet. During the three



RESEARCH AND DISSECTING ROOMS
DEPARTMENT of ANATOMY

Fig. 1.

years that the laboratory has been opened, students have developed a morale which enables us to trust them with the models. And, considering the amount of handling they have had, the breakage has been remarkably small. Among other things the museum contains the usual sets of teaching models of His manufactured by Ziegler of Frieburg, and Steger of Leipzig.

PREPARATION OF MATERIALS.

The embalming-room is situated in the basement, and is reached by a private driveway, which secures privacy in the reception of cadavera. The embalming-room is provided with a hydraulic-pressure apparatus, modeled after the one in the anatomical laboratory of the Johns Hopkins University. It consists of an ordinary water-boiler, provided with controlled outlets and intakes, a pressure gauge and a pipe at the top to conduct compressed air. The embalming and injection fluids

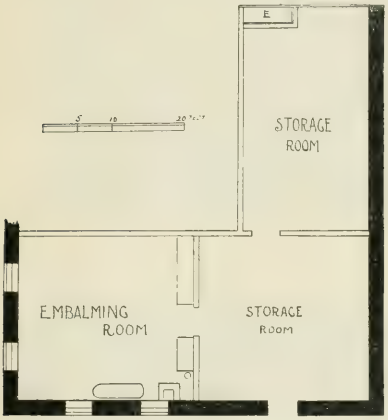


FIG. 4.—PLAN OF EMBALMING AND STORAGE ROOMS.

are forced from aspirator bottles, through rubber tubing canulæ, into the body at any desired pressure. The material received by this department comes almost exclusively from the Almshouse. The subjects are, as a rule, very old, and owing to the activity of certain religious organizations which insist on the burial of females, consist almost exclusively of males. The embalming is done through both distal and central ends of the femoral arteries. At first, we embalmed from one side alone, but experience soon showed that the advanced degree of arterio-sclerosis in these subjects often made it impossible to preserve both extremities well unless the injection is made through both femorals. The fluid is forced into the vessels from the injection flask under a pressure of about five or six pounds to the square inch, by means of a series of Y-tubes terminating in cannulæ. After the body is injected it is allowed to remain for 24 hours, and then coloring matter is forced into the vessels. At first both arteries and veins were injected; subsequently the venous injection was abandoned, as the inevitable tearing of small veins in order to clean up a dissection gave it a very dirty appearance. With the single arterial injection, these vessels stand out clearly differentiated from the collapsed veins, which can be easily seen and preserved in an average dissection. After the vascular injection is complete, the calvarium is opened and the brain removed for use in the course in neurology, in which each student sections at least one complete encephalon. Several methods of embalming have been used. The earliest was an arsenic-formalin mixture which preserved the body excellently; but, like most formalin embalming fluids, tended to make the arms and legs stiff and rigid. The abduction of the extremities necessary for the dissection of the axilla and perinæum frequently ruptured the pectoralis major and the abductors of the legs. Moreover, this material frequently became discolored, the differentiation between the muscles and the surrounding structures was not distinct, and finally they seemed to be particularly liable to infection with moulds. Struther's fluid was also used, and in many instances gave great satisfaction. In cadavera preserved by this method the differentiation of the fascia is exquisite; but, in many of them, the coagulation of the myosin is incomplete, leaving the smaller muscles soft and friable. Thus it became quite difficult to preserve them without tearing or distortion throughout the dissection of a part. The carbolic mixture advocated by Mall we employ now almost exclusively. By its use the preservation and differentiation of the various structures seems on the whole best. Moreover, bodies preserved by this method are practically odorless, and can be left exposed to the air for months during dissection without either moulding or undergoing putrifaction. The material has been preserved in two ways, one in wood alcohol vapor and the other by means of immersion in a 3 per cent solution of carbolic acid. For both purposes, zinc-lined wooden tanks are used, varying in capacity from 7 to 14 bodies. The most convenient tanks, in our experience, are 50 inches wide, 27 inches deep, and 6 feet 4 inches long. These tanks have a capacity of 14 bodies. After a careful comparison it seems that the wood alcohol vapor, while efficient, is more expensive and also has the disadvantage of allowing an extreme mummification of the extremities to take place. In bodies, however, where the hands and feet have become almost completely desiccated, or where the skin is tough and leathery, after they have been exposed to the vapor of wood alcohol for a period of two years, we have succeeded in restoring flexibility to the extremities by means of immersion in hot water. When bodies are in this condition, we place them for a period of 12 to 48 hours in a porcelain bath-tub full of water at a temperature of about 60° Centigrade. The fluid is taken up and the hands and feet rapidly soften. By far the best of our material, however, has been that preserved by immersion in a 3 per cent solution of carbolic acid. At present we have over 100 bodies stored in this way, some of which have been in the fluid for eighteen months. The skin becomes particularly well fixed, rendering it useful in the preservation of material from desiccation through a large portion of the period of dissection. The method also has the advantage of being economical. A string

is tied around the neck of each subject to which is attached the body number held upon a cork. This floats upon the surface of the tank. It is possible, therefore, by simply referring to our card catalogue of anatomical material to recover any body at will. Above the tanks is a rail suspended from the ceiling; a wheel to which is attached a block and tackle travels on this track. It is a simple matter for one person to handle and care for the material by means of this tackle. An elevator runs

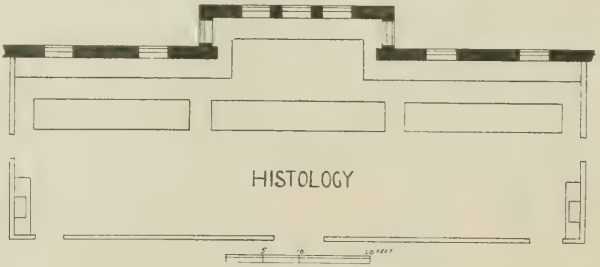


Fig. 9.—Plan of Histological Laboratory.

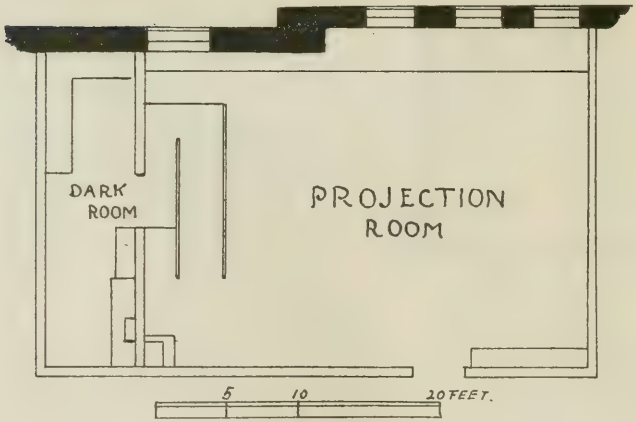


Fig. 11.—Plan of Projection Room.

from the storage-room in the basement to the dissecting-rooms on the top floor. In the embalming-room, there is also a macerating tank, for the preparation of skeletons from the finished dissections.

The Preparation Room and the Research Rooms.

On the top floor, in a wing opposite the amphitheater and dissecting-rooms, are the research rooms and preparation room. The latter is large and has abundant light from three sides as well as the roof. It was planned with the idea of its being the main working center of the laboratory. In this room are the commoner materials and reagents for all ordinary work and the simpler forms of research. The preparation room is also intended to simplify as much as possible the routine work of the department. It is in charge of the technical assistant who prepares the sections for class work and keeps the stock solutions, reagents, and stains always in good condition. The room is provided with large unit tables, lockers for reagents and apparatus, thermostats, glass tubing and rodding, the still, and a large sink with numerous gas and water attachments, microtomes, museum jars for stock specimens, blast apparatus, vises, etc. Acid corrosions are made on extension shelves just outside of the windows, which do very well in lieu of a hood. There is also a large scale stand provided with coarse and fine balances.

The research rooms are occupied by individual members of the staff, and have, besides the usual water and gas supply, the equipments which the several members require for their own special work.

Histological Laboratory.

The histological laboratory is situated on the second floor, and was made by tearing down two partitions and converting three rooms into one. The room faces the north and abun-



FIG. 2.—DISSECTING ROOM.



FIG. 3.—MODEL ROOM.



FIG. 5.—EMBALMING ROOM.



FIG. 6.—STORAGE TANKS AND ELEVATOR.



FIG. 7.—PREPARATION ROOM.



FIG. 8.—PRIVATE ROOM.



FIG. 10.—HISTOLOGICAL LABORATORY.

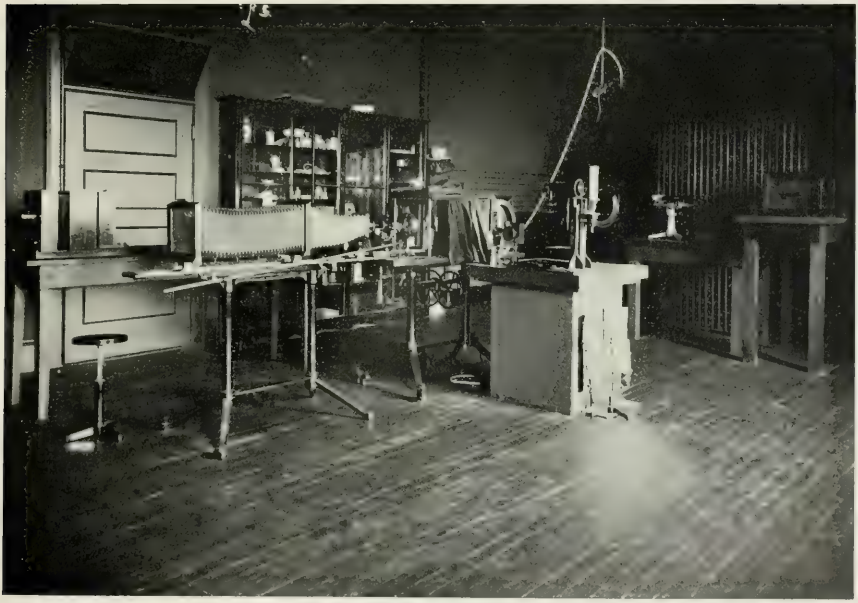


FIG. 12.—PHOTOGRAPHIC ROOM.

dant light was obtained by cutting two extra windows in the alcove. Students are seated either at wall-shelving or at long tables. The room has a capacity for fifty students at one time. There are two large sinks, a large paraffine oven with apartments for each member of the class. On the opposite side of the hall is a small room used for the storage of charts and microscopes. Each student is provided with a wall locker to which he carries a key. This locker contains his microscope, reagents and working equipment; a small wooden tray with holes that exactly fit the reagent bottles makes it easy for him to remove his reagents from the locker to the desk. Each locker outfit contains the simpler reagents and stains, while those that are only used occasionally are kept on the shelves above the sinks. The microscope outfit consists of a Leitz 1-A stand, with the 1, 3, 5 and $\frac{1}{12}$ objectives and the 0, 1, 3 and 4 oculars. Each student has, as well, a dissecting microscope for teasing purposes and low power work. The general equipment of the room consists of a stereoscopic microscope for demonstration purposes, microtomes for both paraffin and celloidin sections and a well-stocked cabinet. Most of the histological models are kept in the general model room. We have used bromide enlargements for our charts in microscopic anatomy. These are made from plates or figures from the literature illustrating the objects which it is desirable to show. They are very clear and are much cheaper than charts made by an artist.

Projection Room.

The projection room is in the basement where the inconvenience of its situation is compensated for by the existence of brick piers erected independently of the building. These facilitate the making of photographs without the occasional annoying tremor caused by passing tram-cars. The walls and ceiling of the projection room are black, while the windows are protected with two sets of opaque curtains which entirely exclude the light when the room is used for projection. The room is equipped with a complete Zeiss microphotographic apparatus, consisting of bellows, plate-holder, microscope, condensers, filters, stand, etc., etc. The Zeiss apparatus is the property of the Department of Pathology and is used by both departments in common. Owing to the fact that there is no electric current in the building we were at first forced to use a cluster of Welsbach lights for microphotographic work. And while fairly successful pictures could be taken with this illumination, they were not wholly satisfactory, as the peripheral illumination through the higher powers of the microscope was vague. More recently we have employed a 3-burner acetylene lamp. With this light, we succeed in obtaining clear pictures with high magnifications. Successful projections up to 100 diameters can also be obtained by its use. The acetylene generators are now manufactured so they are safely, cheaply, and easily operated. Besides the Zeiss apparatus there is a large 8 x 10 copying camera, fitted with a 5-foot draw and bellows. This is equipped with a Zeiss protar lens. There is also a small Zeiss camera, 5 x 7, with a complete series of lenses for various grades of minor work.

Adjacent to the projection room is the dark-room, provided with a maze-doorway, by means of which it is possible to enter and leave the dark-room at will without closing a door. The light for the dark-room is situated in the projection room, thus it is easy to keep the former cool. A light-tight ventilator has also been arranged in the transom of the door in the dark-room, giving with the maze-entrance a constant current of air. It is possible, therefore, when occasion requires, for this room to be in use six or eight hours a day without having the air become either close or oppressive. I have tested the dark-room by leaving half a plate exposed for ten minutes in the doorway, while the other half was developed immediately for comparison. At the expiration of the time stated, absolutely no fogging was observed in the half of the plate used for the test.

Unit System of Furniture.

As far as possible, the laboratory is furnished throughout on the unit system. Wall cases, museum cases, dissecting tables, laboratory tables, operating tables, wall shelving, sinks, book-stands, animal cages, etc., are all constructed on a unit system, making the rearrangement of the laboratory furnishings easy and practical. The furniture is stained a cherry red, while the table tops, sink tops, etc., are all stained with anilin black. Although the preparation of furniture by this latter method is rather tedious, the results amply justify the extra expenditure of energy. They are a dead black in color, are not acted upon by acids, alkalies, alcohols or any of the reagents used in ordinary anatomical work. After this treatment the furniture always looks well, and is easily kept clean. The process is so simple that an experienced painter is unnecessary, as any janitor can prepare the woodwork by this method. Three solutions are necessary:

Solution No. 1.	cc.
Anilin Oil	1.5
HCl	1.5-1.75
Water	1000

There should be sufficient HCl added to make the solution slightly acid. It is shaken until the oil globules no longer float on the surface, which occurs when the solution is slightly acid.

Solution No. 2.	cc.
Sodium Chlorate	100
Copper Sulphate	100
Water	1600
Solution No. 3.	**cc.**
Chromic Acid	5
Water	100

Paint with solutions No. 1 and No. 2 alternately three or four times, allowing each successive coat to dry thoroughly. One or two coats of solution No. 3 will then turn the wood perfectly black. After the surface is entirely dry, it may be rubbed down with boiled linseed oil or better with a 5% solution of paraffin in benzine. If the paraffin solidifies or crystallizes out, the surface of the table may be warmed with a Bunsen burner and the melted paraffin rubbed into the wood.

ANATOMICAL MATERIAL—ITS COLLECTION AND ITS PRESERVATION AT THE JOHNS HOPKINS ANATOMICAL LABORATORY.

By Franklin P. Mall.

In 1893 when the Medical Department of the Johns Hopkins University was opened, it was announced that the course in gross anatomy would be largely practical and that the work would begin on November 15. At the beginning of the session, in October, it was found that no cadavers were on hand, nor were the chances in favor of obtaining them good, for during the previous year but 49 subjects came through the regular channels, to supply the some 1200 students in the different medical schools of Baltimore. The problem now changed from teaching anatomy to obtaining cadavers for a new school, and only complicated the situation by adding more students to a number already far too large to be supplied. I soon learned that during the fall of the year the demand for cadavers by the seven schools was far greater than the State supply and that the additional irregular subjects did not ease the situation very much.

Several years before, a case of burking, followed by a scandal, aroused public opinion sufficiently to enable the Legislature to pass a law regulating dissection, after the bill had been introduced a second time and pushed with great vigor. This law, unfortunately, is a broad compromise, one which will not compel the leading officials to deliver the bodies of the unclaimed dead to the Anatomical Board, nor does it make it a legal offense to remove a corpse from the Public Cemetery. So in order to become operative in the direction in which the law was intended, *i. e.*, to give the bodies of paupers to the medical schools for dissection and thereby to prevent trafficking in them, it is necessary to have the good-will of the Health Commissioner and a strong Anatomical Board. At first a few bodies were delivered to the Anatomical Board but, as a rule, the pauper dead were claimed and buried at the expense of the city, or if "unclaimed" were also often buried by the city because it was difficult to determine whether the deceased had been a resident of the State for a year prior to his death. So by this interpretation of the law the Health Commissioner saw his way clear to send 49 cadavers to the Anatomical Board during the college year 1892-93.

During October, while waiting for dissecting material, I experimented upon dogs with all kinds of embalming fluids in order to have the best possible method for cadavers when obtained. I may add that during the six weeks these experiments were being made the bodies of all the dogs putrefied with the exception of those embalmed with carbolic acid. At this time the weather was unusually hot, even for Baltimore, and I made a sufficiently large number of experiments to decide in favor of a carbolic acid mixture as the best embalming fluid. This experience proved to be valuable, for we have ever since been able to embalm our subjects well and in turn the method has spread to many of the medical schools of America.

We were to begin to dissect on November 15, and before the date arrived the students began to worry, for they knew we had no subjects, and they also knew that they were not to be obtained. I myself felt very much the same in case we depended upon the State to send cadavers, and all preparations were made to go to larger cities for aid, which is easily obtained with a large purse. While these preparations were being made we postponed work until the 16th, and then the 17th, when, late in the evening, a subject was left in the basement. The next day one came from the State, and a few days later another appeared in the basement. This made us safe until Christmas, or until Easter, provided we dissected carefully and preserved the specimens well.

Towards Christmas, when all of the dissecting-rooms of Baltimore were under way, it was found that cadavers were more abundant and we did not fail to take what came, embalm them well with carbolic acid and place them in a large ice box which had been constructed in the meantime. By spring the box, which was built to hold five cadavers, had in it twenty and the further supply was not taken.

By this time it became apparent that in future it would be well to have an abundance of subjects on hand, and during the second year of the Medical Department an Anatomical Laboratory was built in which was placed an ice machine with a cold-storage vault large enough to hold 60 subjects. During the summer just 50 subjects were received, which together with 8 on hand nearly filled the vault. We also found that it was much cheaper to operate an ice machine than it cost to keep the large ice box filled with ice during the previous summer.

Shortly after the cold-storage apparatus was in operation the Anatomical Board proposed that all the subjects received by it during the summer should be stored in the Anatomical Laboratory. Heretofore these had been buried and were just so much loss to the Board. The Table on the following page shows in a measure the advantages of this arrangement by the gradual increase in the number of cadavers from year to year. I gather from the records of the Board that the total number of adult subjects delivered by the State have averaged 300 a year during the past five years, thus multiplying our supply sixfold, since we receive and preserve every subject. Furthermore, there are the bodies of about 300 infants which are also used extensively, making 600 in all, which would be enough to supply the demand were there not a gradual increase of the total number of medical students in Baltimore from year to year.

TABLE GIVING THE RACE AND SEX OF THE CADAVERS ARRANGED IN HUNDREDS.

The dates of the reception of each hundredth subject, the number of autopsies, the source of the cadavers, and the number of bodies returned to friends are also given. The first cadaver was received on Nov. 17, 1893.

Number in hundreds.	Date of Reception of each hundredth Cadaver.	Race not given.		Negro.		European.		Autopsy.	Number received from "outside sources."	Number returned to friends.
		Male.	Female.	Male.	Female.	Male.	Female.			
100	Oct. 12, '95	41	11	30	16	9	3	30	45	0
200	April 16, '97	3	2	42	21	25	7	25	27	2
300	Oct. 16, '97	3	0	40	21	32	4	43	50	0
400	May 26, '98	3	0	37	26	31	3	44	28	1
500	Oct. 10, '98	0	1	38	31	25	5	44	2	0
600	Mch. 18, '99	0	0	48	16	29	7	53	1	0
700	July 26, '99	3	8	43	21	21	4	34	0	1
800	July 13, '00	0	10	43	19	26	2	31	0	0
900	Feb. 27, '01	1	0	36	26	28	8	33	0	3
1000	June 10, '01	1	0	54	18	23	4	49	0	4
1100	Oct. 31, '01	0	0	50	21	24	5	37	0	2
1200	July 3, '02	0	0	42	31	24	3	41	0	5
1300	April 6, '03	0	0	42	21	37	10	43	0	10
1400	Nov. 26, '03	1	1	47	25	21	8	41	0	3
1500	April 12, '04	0	0	44	27	25	4	30	0	6
1600	Aug. 13, '04	0	0	44	32	27	7	33	0	5
1641	Oct. 1, '04	0	0	17	8	13	3	13	0	2

In 1897 a new Health Commissioner, Dr. Jones, was appointed and his order was "that all bodies should be turned over to the Anatomical Board for disposal, and if they were not wanted should be buried in the Public Cemetery." Although the cadavers received at the Johns Hopkins are not the total number received by the Anatomical Board during the year, they are in a measure a proportion of the whole, for they include a certain per cent of those collected during the winter and all of those of the summer. During the four years preceding Dr. Jones' appointment the Anatomical Board sent to the Johns Hopkins for storage an average of 44 subjects, while during the time he was Commissioner of Health the average rose to 185, which has been maintained ever since. Shortly after Dr. Jones' appointment I was elected Chairman of the Anatomical Board (October, 1898), and immediately took steps to complete the work Dr. Jones had begun. Orders were issued to the medical schools not to accept cadavers from outside sources, for there was an abundance of them on hand, and a form of receipt was introduced by which a cadaver could be traced had it gone astray. So since that time no cadavers have been procured from outside sources for dissection, for the "go-between" has had neither stock nor buyer, for all of the unclaimed dead go directly to the Anatomical Board.

The receipt enabled the Anatomical Board to keep the accounts up to date from a business standpoint. Before this there was no great haste in rendering bills nor in paying them, but from now on accounts were balanced once a month and any discrepancy could easily be corrected, for the details were still fresh in mind. Since the trafficking in dead bodies was effectually broken up in Baltimore, the one source of danger, *i. e.* sending bodies beyond the borders of the State, had to be watched and it was this receipt which proved to be of value in finding and convicting an offender several years later (see Devine case). From this time on the receipts became official and are stored in the Health Department.

The business side of the Board is now in good running order, being in the hands of a secretary appointed by the Chairman of the Board, who in turn is elected annually by the Board. When I became Chairman, Dr. Warfield, my predecessor in office, handed over to me bills for nearly $1000, one-half of which had been paid in advance by him. I immediately sent out bills and thereafter made a settlement once a month, collecting from the schools receiving them $4 for each whole cadaver and $2 for each autopsy. At the end of the first year we had no debts and $123 in the treasury, and a year later $673, which has been increasing in amount ever since.

We are now obtaining all of the cadavers within the scope of the law, are dividing them according to legal requirements, have our treasury in good condition, are watching those who desire to cut into our supply (a certain type of burial society), and cooperate with the Health Department. Now, instead of having a column in our records of which we can give no account, we can account for every cadaver and often bodies are temporarily stored with us to be returned to friends when so ordered by the Commissioner of Health. During 1903 fifteen such bodies were returned, and during 1902, one which we had had in storage for eight months.

It is evident from what has been said above that the collection of cadavers for dissection was greatly facilitated when they were carefully embalmed and stored, for by so doing they could be collected during the summer, or whenever in excess, and kept until there was a demand for them. From a small beginning with an ice box holding five cadavers, a vault was built, and shelved to hold sixty cadavers. Later, the shelves were removed and the bodies were stacked, which proved to be better for the bodies, at the same time increasing the capacity of the vault six-fold. During these ten years we have had considerable experience in operating a small ice machine, in aiding to construct new plants elsewhere and in the different methods of embalming cadavers with carbolic acid. The problem presents different aspects according to the intelligence of the embalmer and the number of subjects to be embalmed each week. If there is a small number, say 50 a year, it is a question in my mind whether it is economical in time and expense to preserve cadavers by means of cold-storage. If the number per year is over 100, *i. e.*, at least 50 to be stored constantly, refrigeration has decided advantages.

At first the bodies were injected with 2 liters of a solution of equal parts of carbolic acid, glycerine and alcohol. I constantly came back to this solution, for it is easily handled and but small quantities are needed. But it is found that with so small a quantity but little of it reaches the feet, while most of it lodges in the viscera. So the quantity was gradually increased until from 4 to 6 liters were used, which means about 3% of carbolic acid to the body weight. Even with this quantity enough acid rarely reaches the feet, so it was necessary to change the method and inject the embalming fluid into the legs. At first but one femoral artery was used,

but in such cases it was difficult to force enough of the fluid into the arteries of the foot of the opposite leg. So, thereafter, cannulæ were introduced into the femoral arteries of both legs, and the legs were first injected and then the body. In making these injections a constant pressure is used, from 150 to 200 mm. Hg., for this is much more certain than the irregular pressure given by a syringe.[1] In cadavers preserved in this way all parts are well embalmed, provided clots of blood have not blocked any of the arteries. Most of the muscles are coagulated in cadavers prepared as described above, and this is desirable in case they are to remain in the dissecting-room for a long time. If less acid is used the muscles retain their normal color and consistency, but the preparation becomes infected easily and decomposes in warm weather. Furthermore, the moisture required to keep the preparations from drying hastens the decomposition.

It was also found that the hands, feet and face dried easily in the dissecting-room, and especially in cold-storage, and to prevent this the body was carefully wrapped immediately after the embalming process was ended. First the hands, feet and face were smeared with vaseline and wrapped with bandages of tissue paper which is ordered from the mills in rolls 5 inches wide and 3 inches in diameter. Then these bandages and the rest of the body were smeared with vaseline and the whole carefully wrapped with bandages of cheese-cloth about a foot wide. It is well to wrap the legs and arms separately in order that they may be exposed easily for dissection, the rest of the body remaining wrapped, for the covering is an additional protection in the dissecting-room. Such bodies may be retained in cold-storage indefinitely without drying, although the thorax and abdomen gradually lose much of their moisture.

Immediately after embalming and before the body is wrapped the arteries are injected with pigment. For this purpose it is desired to have granules which fill the finer arteries but do not enter the capillaries. The arteries of the first 200 cadavers were filled with red-lead and plaster-of-Paris, but it was found that the injection was often incomplete and in addition the action of the carbolic acid caused the color of the lead to turn black. Experiments were then made with all kinds of granules and fluids and it was soon found that granules of ultramarine blue mixed with shellac and alcohol proved to be the best. The granules are cheap, are just small enough to pass to the finest arteries; the solution is injected cold, and can be kept in stock constantly. It sets in the course of a month which is no disadvantage, for we rarely dissect fresh bodies. No attempt is made to distend the larger arteries, but it is desired to fill the many smaller arteries, as those of the periosteum and of the skin. Keiller accomplishes the same with chrome-yellow and gelatin but his cadavers are embalmed with a formalin solution which causes the gelatin to become insoluble and tough. Apparently his results and ours are about the same.

About 1000 cadavers were embalmed by injecting each with 5 or 6 liters of a 33% solution of carbolic acid as described above. The vessels were colored with the ultramarine shellac solution. They were then vaselined and wrapped and kept in cold-storage until needed. But it was found that occasionally an extremity was not well embalmed and frequently the epidermis would macerate and peel off with a subsequent putrefaction of the skin. Often it would soften and peel off, especially from the hands and feet after they had been kept wrapped for a long time in the dissecting-room. To obviate this the parts had to be watched and in case the artery was found plugged it was picked up and injected a second time. The skin was also treated with a solution of glycerine, carbolic acid and water and in extreme cases with the original embalming fluid. This, however, was found to be inconvenient and unsatisfactory, so we began systematically to try and remedy the defect. Struthers[2] had already met this difficulty by painting the cadavers with carbolic acid and glycerine (1 to 8) a number of times, say 3 or 4, to embalm the skin from without, or in other instances by injecting the same solution hypodermically. This is inconvenient when many cadavers are to be painted, especially when but a few of them are to go to one's own dissecting-room, so I began by immersing the whole body in different solutions of carbolic acid after the arteries had been injected. It was noted above that in embalming a cadaver it is best to inject exactly 3% of pure carbolic acid to the weight of the cadaver in order to obtain the best results, and upon experimentation I found that the same strength gave the best results in a tank. A 4% solution is too strong and in a 2% solution the skin macerates and the epidermis falls off. Dr. Bardeen also obtained the same results with embryo pigs which are used in great number in our laboratory, and recently Keiller has confirmed Struthers' results with hypodermic injections. Keiller, however, uses large quantities of an aqueous solution of carbolic acid and injects it until the body is very œdematous. In all cases the principle and the results are the same.

The experiments with the vat were frequently made upon the subjects between Nos. 900 and 1300, at first upon single cadavers and later with 10 at a time. It was found that cadavers which were evenly embalmed, epidermis included, with a 3% solution of carbolic acid and wrapped with carbolized vaseline could be kept upon an open shelf in a warm room at Baltimore for at least 6 months and still be perfectly good for dissection. A cadaver prepared in this way cannot be detected from others by its quality or appearance. It should be possible to keep them indefinitely in an aseptic room with an atmosphere saturated with moisture. But to make the method easy two large tanks holding about 4000 liters each were constructed, which were half filled with a 3% solution of carbolic acid. Each holds about 15 cadavers. First, one was filled with cadavers that had been embalmed in the usual

[1] Professor Keiller (Phil. Med. Jour., Dec. 29, 1900) distributes the carbolic acid evenly by injecting a large quantity of aqueous solution into the carotid, and also hypodermically, until the whole skin is distended. His results are practically identical with ours, differing only in the per cent of acid to the bodyweight.

[2] Struthers, Edin. Med. Journ., Oct., 1890.

way, and then the other. All the cadavers are then taken from the first tank, vaselined and wrapped and placed in cold-storage. The water of the first tank has lost some of its carbolic acid which is to be replaced. An easy method to ascertain this loss is to determine how much carbolic acid 100 cc. of the filtered solution will take up and to compare it with the amount required to saturate 100 cc. of water. If at a given temperature it takes 4 cc. of the straw-colored carbolic acid to saturate 100 cc. of water and 2 cc. to saturate 100 cc. of the filtered fluid under test, then one per cent must be added to the tank to bring it back to a 3% solution. When the first tank is full of bodies the second is emptied, the bodies being wrapped and stored and the fluid of the tank strengthened. And so on. At the rate we receive cadavers they remain in these tanks from 3 to 6 weeks, long enough to allow the carbolic solution to penetrate them from 2 to 4 centimeters. I may add that we use the straw-colored carbolic acid (strength 92 to 97%) which is cheap and is as good for the vat and for the arteries as is the more expensive crystalline form.

Beginning 18 months ago (with No. 1300) each cadaver was embalmed with 6 liters of a 33% solution of carbolic acid, injected with about 2 liters of shellac alcohol and ultramarine blue, immersed in a 3% solution of carbolic acid for 3 to 6 weeks, vaselined and wrapped, and preserved indefinitely in cold-storage. At present we are constructing an underground vault to be carefully cemented with water-proof cement and large enough to hold 150 bodies. In case cadavers can be kept indefinitely in a 3% solution of carbolic acid, I see no reason why our cold-storage apparatus should be replaced when it is worn out.

It appears to me that carbolic acid is by all odds the best preservative for cadavers for dissection. It is easily injected and diffuses rapidly and extensively. So great is the power of diffusion that the heads of autopsy subjects, which are not injected, are preserved by the carbolic acid which diffuses from the trunk. It is also the best solution in which to keep cadavers. It is also antiseptic, so much so that I have never seen the slightest sign of an infected wound in our dissecting-room, and does not injure the instruments. It is not necessary to pay any attention to slight wounds for they heal more rapidly in the dissecting-room than elsewhere, when the bodies are embalmed with carbolic acid. Finally, it is inexpensive. A gallon of straw-colored acid costs but 40 cents, and half this amount is enough to preserve a cadaver for several years, and the other half will make enough 3% solution to immerse it.

Alcohol and glycerine are also excellent preservatives, and possibly more glycerine would improve the embalming fluid somewhat. It is especially valuable in keeping the dissection from drying too rapidly while the student is at work. However, in order to prevent drying the student swabs the dissection whenever necessary with a 10% solution of glycerine in alcohol (see Gerrish's Anatomy), with which he is supplied. By this method it seems to me that the glycerine reaches the right place, while when it is injected much of it is wasted. When the student leaves his work he covers the dissection with a dozen thicknesses of moist (not drenching-wet) cloths, and all is again covered with water-proof sheeting which is prepared by saturating domestic or duck with boiled linseed oil as recommended by Keiller.

When the subjects are ready to be stored each is marked with a special tag, which cannot be duplicated, and is delivered on the desk of the instructor in charge of the vault when the cadaver is sent out of the laboratory or to the dissecting-room. The first 1000 are marked A, the second 1000 B, and so on. Each body is also recorded in a book, which the janitor keeps, and upon a card, which is here reprinted, for the instructor in charge. Once a year an inventory is taken and the cards are stamped with the inventory date. Thus every precaution is taken to keep track of the bodies.

JOHNS HOPKINS UNIVERSITY

ANATOMICAL LABORATORY

No..... Name..... Age.....

Length..... Weight.....

Date of Death.....190 Cause of Death.....

Received.....190

SEX	COLOR	AUTOPSY	QUALITY
Male Female	White Black Mulatto	Yes No	Fat Medium Lean

Transferred to.....

Injected with.....quarts of.....at.....inches pressure.

Arteries injected with..... at.....inches pressure.

Put in.....% Carbolic vat..... ...190

Transferred to Cold Storage.....190

Embalmed by.....

At first it was impossible for me to obtain easily the names and data of the bodies, but I had the color, sex and quality carefully recorded. These records often proved to be of value while making studies and in identifying bodies in case they were sought by friends. After No. 767 the names and ages are recorded. The cause of death is given after No. 901. The length and the weight of the body together with the intermediate color, mulatto, is recorded after No. 1448.

The Table on the following page gives a list of the cadavers which have been stored up to October 1, 1904. It shows how many bodies were used within the first year after they were received, within the second, and so on. The more recent subjects are all rated to October 1, 1904, so the 15th and 16th hundreds appear to have been used, while in reality most of them are still on hand. It will be noticed that under 400 a subject was kept for 5 years, and in the dissecting-room this cadaver proved to be as good as any of the fresher ones. A number were kept 4 years and in no case did the students suspect that they were dissecting subjects which we had had on hand so long. Under 500 a subject was kept 7 years and this we still have on hand. Generally, it is our aim to dissect cadavers which we have had on hand for two or three years, while the fresher cadavers are sent by request to other medical schools. Our experience demonstrates conclusively that cadavers preserved in cold-storage for several years are more satis-

factory for dissection than are fresh ones, and there is no reason why they cannot be preserved in this way indefinitely in case they are packed closely to prevent evaporation. This we now accomplish by stacking all of the old cadavers on one side of the vault with an air-space around the pile, and then the fresh cadavers are laid closely on a platform on the other side of the vault, and when this has frozen a second layer is placed over it, and so on. The wrapping prevents the subjects from freezing together firmly.

TABLE SHOWING HOW LONG THE CADAVERS WERE KEPT IN COLD STORAGE BEFORE BEING DISSECTED.

They are grouped in hundreds. The first column gives the number that were used during the first year. The records are carried to October 1, 1904.

Number of cadavers in hundreds.	1 year.	2 years.	3 years.	4 years.	5 years.	6 years.	7 yrs.
100	69	25	2	3	1	..	..
200	72	19	8	1	..	..	..
300	71	22	5	2	..	..	..
400	67	23	9	0	1	..	..
500	31	49	19	0	0	0	1
600	49	40	9	2	..	..	..
700	74	26	..	..	..	..	..
800	41	59	..	..	..	..	..
900	39	59	2	..	..	..	..
1000	29	61	9	1	..	..	..
1100	80	13	6	1	..	..	..
1200	76	19	5	..	..	..	..
1300	51	36	13	..	..	..	..
1400	27	73	..	.	..	..	..
1500	100	..	..	..	..	..	..
1600	100	..	..	..	..	..	..
1641	41	..	..	..	..	..	..

A Word Regarding Cold-storage.—The first cold-storage apparatus for the preservation of anatomical material was installed by Professor Huntington at Columbia University, about 1893. His apparatus was operated from a large central plant and was by no means inexpensive. Our vault was the second and was constructed early in 1895. The problem at the Johns Hopkins was different, for it was necessary to put in all of the machinery, which on account of the additional expense could not be operated during the night. In order to make this possible the brine tank was set up within the vault and from this the brine was pumped through pipes along the ceiling. When the machine was not in operation the large amount of cold brine within the vault was adequate to absorb much of the heat which entered, thereby keeping the temperature well below the freezing point. We found that we had planned so well that it was necessary to operate the machine but once or twice a week during the winter and but six hours a day during the hot summer to keep the temperature well below 32° F. all the time.[2] Had the surface of the brine tank been larger it would have been possible to keep the temperature of the vault below 32° without circulating the brine through pipes suspended from the ceiling. So at my suggestion a number of recent apparatuses have been constructed with three or four very narrow brine tanks set around the side of the vault, without any brine circulation. By this arrangement it is found that the temperature of the vault can be kept with ease below the freezing point. Vaults constructed in this way are to be found at the University of Pennsylvania, at Cornell University and at the University of Wisconsin. The vault at the University of Wisconsin is the most recent and was designed by Prof. Miller. It is built of porcelain brick, no wood being used in its insulation and all sides of the vault are lined with narrow brine tanks extending from the floor to the ceiling. Throughout it is a dry vault, which favors its insulation, so much so that during the hottest weather its temperature rises but 3° in 24 hours, with the ammonia turned off. As far as I can see it should last indefinitely, for the compressed ammonia is supplied from a distant plant, so there is no machinery to get out of order. Under these conditions cold-storage vaults are certainly much more desirable for the preservation of cadavers than carbolic acid vats.

[2] See Mall, Arch. Anz. XI and Johns Hopkins Hospital Bulletin, 1896.

THE DEVELOPMENT OF GRAVE ROBBING IN ENGLAND.[1]

By G. Canby Robinson, M. D.,
Pennsylvania Hospital.

In England, by Act of Parliament in 1540, four executed criminals were given yearly to the Barber-Surgeons for dissection, and twenty-five years later, Queen Elizabeth granted the bodies of four felons executed in Middlesex to the College of Physicians of London "that the president or other persons appointed by the college might, observing all decent respect for human flesh, dissect the same." In 1663 Charles II increased the number of criminals to be annually dissected to six, and in 1752, Act of 22, George II required dissection or hanging in chains of bodies of all executed murderers in order that "some further Terror and peculiar mark of Infamy might be added to the Punishment of Death." This Act, although no doubt an aid to the advancement of anatomy for the time being, produced in England a deep-rooted association of the dissection of the body after death with some serious crimes committed before death, and so strengthened the public feeling against the dissection of unclaimed pauper dead. This was a potent factor in hindering the passage of an anatomy act in England.

[1] Extracts from a paper read before the Johns Hopkins Hospital Historical Club, October 10, 1904.

Let us now consider the growth of the Anatomical Schools in London and Edinburgh, and trace there the fight between a deep-rooted instinct to protect the dead and the scientific spirit which demanded subjects for dissection.

The teaching of anatomy in England, which was first attempted in a well ordered manner a short time before 1600, was conducted entirely by a few corporate bodies of which the Company of Barber-Surgeons and the College of Physicians of London were the most important. The bodies of criminals provided by law were used. These Public Anatomies, as they were called, when held by the Company of Barber-Surgeons, took place in the Hall of the Company, and were conducted with much pomp and ceremony. Attendance upon them was compulsory to the members of the Company, they being fined when absent. The Public Anatomies were held usually four times a year, and three bodies were dissected each time, one to show the muscles, one to show the bones, and one to show the viscera. Private anatomies were forbidden by the Company. In those days when executions were much more frequent than to-day, and when the method of teaching was such that a few bodies sufficed, the law provided a sufficient number. Even at this time, however, certain broad-minded, thoughtful people, having in mind the great benefits to mankind to be derived from a widespread knowledge of anatomy, bequeathed their bodies for dissection, in order to aid in the spread of this knowledge, and to abate the public feeling against dissection.

In the seventeenth century, under the influence of such teachers as William Harvey, interest in anatomy began to increase very much, and gradually more men arose who, like Vesalius, wanted to investigate things for themselves. And so we find that in the first part of the eighteenth century, about 1715, private schools of anatomy began to be established in London. This meant of course that subjects for dissection had to be provided by other than legal means, and here was the commencement of the systematic robbing of graves.

The business of providing the anatomical schools with subjects by grave robbing gradually became a well organized trade in London. The character of the men engaged in this most repulsive and dreadful occupation, can be well imagined. The century ending in 1832, when sufficient material was provided in England by the Warburton Anatomy Act, presents indeed a gruesome page in the history of anatomy. The master pen of Robert Louis Stevenson has described this night prowling grave robber in words that help us to realize what a depraved creature he must have been. "The Resurrection Man—to use a by-name of the period—was not to be deterred by any of the sanctities of customary piety. It was part of his trade to despise and desecrate the scrolls and trumpets of old tombs, the paths worn by the feet of worshippers and mourners, and the offerings and the inscriptions of bereaved affection. To rustic neighborhoods, where love is more than commonly tenacious, and where some bonds of blood or fellowship unite the entire society of a parish, the body-snatcher, far from being repelled by natural respect, was attracted by the ease and safety of the task. To bodies that had been laid in earth, in joyful expectation of a far different awakening, there came that hasty, lamp-lit, terror-haunted resurrection of the spade and mattock. The coffin was forced, cerements torn, and the melancholy relics, clad in sackcloth, after being rattled for hours on moonless by-ways, were at length exposed to uttermost indignities before a class of gaping boys."

The deeds of one of these resurrection men has come down to us from his own pen in the form of a diary. It was published in 1896 by Bailey, Librarian of the Royal College of Surgeons of London, and the book contains besides the diary which gives it its title, "The Diary of a Resurrectionist," an account of the resurrection men in London and a short history of the passing of the Anatomy Act. It is from this book that much of the following material has been gathered.

After several anatomical schools had been established in London, there was much rivalry between them for material. This gave the gangs of body-snatchers an independence of which they naturally took advantage, and a great amount of tact was sometimes necessary to keep them in good humor. When as dawn of day was approaching, these ghouls would stealthily knock at the lonely back entrance which admitted them with their gruesome burdens to the anatomical school, the rule was to pay cash and ask no questions, and with as few words as possible to let them hurry indoors while the cover of night could conceal their muddy clothes and grimy hands, the marks of their profession.

The "Resurrection man" was in a position to do much harm to an unpopular school, and he had many ways of doing it. It is told that one teacher, Mr. Brookes, whose school had incurred the displeasure of the resurrectionists, awoke one morning to find a partially decomposed human body on his door steps, put there by these disgruntled robbers to arouse public indignation against him. On another occasion a subject for dissection was delivered to Mr. Brookes in a sack. Upon investigation the subject was found to be alive, and was probably so introduced into his house for purposes of robbery.

The means used for protecting the graves against the stealing of their contents were numerous. High walls were built on which loose stones were placed, watch towers, as may be seen in the cemetery outside of Dublin, were erected, and "mort safes" or graves covered by strong iron gratings, were used. One enterprising manufacturer published a long advertisement in the daily paper, extolling the merits of Lillie's Iron Coffin. The advertisement commenced by saying that "Hundreds of human bodies will be torn from their graves this season to supply the demand of the anatomical schools of London and Edinburgh." At Crail a house was erected in 1826 in which bodies were put to remain until partly decomposed and so useless for anatomy, and then buried.

This trade in human corpses was not carried on entirely by men, for we find that several of its tricks could be properly performed only by women. A spring gun was sometimes put over a new grave. The sorrowing mother or bereaved widow would appear a few hours after the funeral, and would go to the grave to let fall her mournful tears upon the freshly turned up mound, and incidentally to cut the wires leading to

the spring gun. Then too a woman was especially useful for going to an anatomical school, and there with much grief to find her child or husband, whose body she had heard had been stolen. Nearly overcome by her great sorrow she would have the body removed, to be carried to the next anatomical school and resold, the gang thus gaining two prices for it.

Bodies did not always reach the grave awaiting them, but were sometimes stolen before burial and were sometimes sold by the grave diggers themselves.

As ordinary means of protecting the graves often failed, and as the custodians of the burying grounds could usually in those days be bribed or made intoxicated, a private watch was sometimes instituted over a new-made grave. Between the watchers and the gang of grave robbers, violent fights sometimes took place. An account of such a fight is to be found in an Irish newspaper of 1830, entitled "Desperate Engagement with Body-Snatchers." "The remains of the late Edward Barrett, Esq., having been interred in Glasnervin Churchyard on the 27th of last month—(January), persons were appointed to remain in the churchyard all night, to protect the corpse from the 'sack-'em-up gentlemen,' and it seems the precaution was not unnecessary, for on Saturday night last, some of the gentry made their appearance, but soon decamped on finding they were likely to be opposed. Nothing daunted, however, they returned on Tuesday morning with augmented force, and well armed. About ten minutes after two o'clock three or four of them were observed standing on the wall of the churchyard, while several others were endeavoring to get on it also. The party in the churchyard warned them off, and were replied to by a discharge from firearms. This brought on a general engagement, the 'sack-'em-up' gentlemen fired from behind the churchyard wall, by which they were defended, while their opponents on the watch fired from behind the tomb stones. Upwards of 58 to 60 shots were fired. One of the assailants was shot, he was seen to fall; his body was carried off by his companion. Some of them are supposed to have been severely wounded as a great quantity of blood was observed outside the churchyard wall, notwithstanding the ground was covered with snow. During the firing, which continued upwards of a quarter of an hour, the church bell was rung by one of the watchmen, which, with the discharge from the fire-arms, collected several of the towns-people and the police to the spot, several of the former, notwithstanding the severity of the weather, in nearly a state of nakedness; but the assailants were by this time defeated and effected their retreat."

So we see that this trade, as one would expect, was not without its perils. Conflicts in the cemeteries over bodies were not uncommon, but the fights were usually between two rival parties of resurrection men, and the rivalry between the different gangs that haunted the various burying grounds was intense. In fact it was largely owing to information that these men gave to the police against their competitors that body-snatching reached such great publicity.

The amount of money that could be made in this nefarious trade was an inducement for men to forsake honest but poor-paying trades for it. A body-snatcher testified before the Anatomy Committee of the House of Parliament that during the dissecting season of 1809 and 1810 his gang of six or seven men had disposed of over 300 bodies at the average price of £4, 4s., or about $20.00, thus reaping an income of about $6000.00, or nearly a thousand dollars apiece. The teeth of the subjects were generally sold to dentists, from which source an extra sum was derived.

When anatomical material could not be obtained in plenty by robbing the graves alone, worse crimes were added, in order that the ghouls might have their money. The state of affairs into which this business had grown may be shown by a brief glance at conditions in Edinburgh in the first part of the nineteenth century.

Under the Monros, father, son and grandson, who had held successively the University Chair of Anatomy from 1720 to 1846, the School of Edinburgh rose to first rank. Schools of anatomy outside the University, where extramural teaching was done, were established. One of the most successful of these was conducted by Dr. Robert Knox, who had, during 1828 and 1829, a class of 505 students. The demand for subjects in Edinburgh was of course very great. Bodies brought from £10 to £20 each, and were even imported from England, Ireland and France.

In 1828 Edinburgh was stirred to its foundations by a realization of the extent to which the traffic in human corpses had grown. This realization was brought about by the facts made public in connection with the famous Burke case, an account of which I quote from Hartwell.

"On the second of November, 1828, it was noised about in Edinburgh that a woman had been murdered on All Hallow Eve for the sake of her body, which was found in the dissecting room of Dr. Knox. In the investigation which followed, it was discovered that William Hare, the keeper of a low lodging house in the West Port, and one of his lodgers, William Burke, had within less than a year, committed sixteen murders, and disposed of the bodies of their victims to the teachers of anatomy. The "Burke" method was to suffocate the victim, already dead drunk. Throttling was not resorted to; the nose and mouth were kept tightly closed, and smothering was soon effected. It was impossible to connect Knox with these villains in any way, except as a receiver of stolen goods for the benefit of the public. Hare turned State's evidence, but Burke was found guilty, hanged and dissected. His skeleton adorns the Anatomical Museum of the University of Edinburgh."

Horrible as this crime was, it was not the last to be attached to and to besmirch the name of anatomy in Great Britain, as London was to see another crime almost as dreadful. Another atrocity was needed to arouse the law makers of England to the realization that some efficient means of protecting the graves must be provided. A crime came to light in November, 1831, in London, which created a sensation, Bailey says, equal to that raised in Scotland by the atrocities of Burke and Hare.

Three men, Bishop, Williams alias Head, and May, accom-

panied by a porter, brought a subject for dissection, a boy of 14, to King's College. The appearance of the body aroused the suspicion of Hill, the dissecting-room porter, and apprehending foul play, he notified Mr. Partridge, the demonstrator of anatomy. The porter's suspicions were confirmed by Mr. Partridge. He produced a fifty pound note and said he could not pay them until it had been changed. In the meantime he communicated with the police, who took the men into custody.

In December, 1831, the three men were found guilty of murder and sentenced to death.

The body proved to be that of an Italian boy who made a living by showing white mice. He had been enticed, so the men confessed, into their dwelling in Nova Scotia Gardens, where he was drugged with opium, and then let down into a well until suffocated. They also confessed to the murder of a woman named Fanny Pigburn, and a boy whose name was supposed to be Cunningham. Both of these bodies they sold for dissection.

Fifty thousand copies of the Dispatch containing their confession were sold, and at the execution many persons were injured in the crowd.

The English public were deeply stirred by these crimes. Something had to be done to protect the graves, and to do away with the gruesome traffic that had grown to such a point that the villains engaged in it did not stop short of murder to obtain their merchandise. Various legislative schemes were proposed and one bill providing anatomical material had passed the House of Commons to be defeated in the House of Lords. In August, 1832, however, the famous Warburton Anatomy Act finally passed through both Houses of Parliament to become a law. This Act provided that a license for the study of anatomy should be issued to proper persons and that the bodies of unclaimed pauper dead might be turned over to those holding licenses for anatomical purposes. Burial was required of all bodies by anatomists six weeks after they were received. It was no longer a misdemeanor for one holding a license to have a body in his possession, and there was a very important clause repealing the law, requiring dissection of all executed criminals. Inspectors, one for each country, England, Ireland and Scotland, were appointed by it. This law was a great success and Bailey says of it, "after the passing of the Act the resurrection man, as such, drops out of history; his occupation was gone, and one of the most nefarious trades that the world has ever seen came completely to an end."

We cannot speak at this time of the methods used for obtaining anatomical material in this country, where the settling of the problem is more complex, as a separate law is necessary for each State. It is pleasant, however, to briefly recall the fact that, after a fight of some years, Massachusetts, our most cultured State, passed a liberal anatomy act, legalizing the dissection of unclaimed pauper dead, in February, 1831, a year and a half before the passage of the Warburton Anatomy Act in England, and was the first English speaking community to have such a law.

Although it cannot be denied that body-snatching still exists to a slight extent in this country, yet most of the States have good anatomical laws, which efficiently provide material for dissection. As the robbing of graves passes out of existence, there disappears also the dread and horror with which the public has regarded for hundreds of years the study of anatomy, as the public has learned to appreciate the great importance of sound anatomical training as a firm foundation for all branches of scientific medicine.

ON FLECHSIG'S INVESTIGATIONS ON THE BRAIN.[1]

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The first report made to the Central Committee for the Investigation of the Brain consists of a paper by Paul Flechsig which marks an epoch in the history of the nervous system. This work lays the foundation of our knowledge of the paths in the brain and their relation to the basal ganglia. The work represents the study of serial sections of 56 human brains between the stage when myelinization first begins, four months before birth, and the time when every portion of the cortex shows some medullated fibers and the main paths are laid down, namely, four months after birth. This entire period represents eight months. Through the study of these brains Flechsig divides the cortex into 36 areas, of which the first 12 are myelinized before birth and the rest after birth. The sequence of the numbers represents the time of medullation, and as will be seen the time of birth is not a fundamental division. In general the study of these different zones shows that the first areas in the cortex to become medullated are primary sensory areas representing smell, touch and muscle sense, sight, hearing and taste. The next group of centers to become medullated have at first only fibers within themselves, that is, neither projection fibers nor association bands, so Flechsig calls them automatic centers of unknown meaning. The rest of the areas have association bands and it is most interesting that the earlier zones of this group develop as a marginal zone around the primary sensory areas and first

[1] Flechsig: Einige Bemerkungen über die Untersuchungsmethoden der Grosshirnrinde insbesondere des Menschen. Dem Centralkomite für Hirnforschung vorgelegt. Berichten der mathematisch-physischen Klasse der Königl. Sächs. Gesellschaft der Wissenschaften zu Leipzig, Jan. 11, 1904.

receive short fibers from them. They are undoubtedly connected with the sensory areas in function. The last three zones develop long association bands first and are the great association centers. This will be summed up in the following classification.

I. Primary areas.
 1. Areas with primary sensory projection fibers. 1, 2, 4, 5, 6, 7, 8, 15.
 2. Areas without primary projection fibers; mostly automatic unknown areas. 3, 9, 10, 11, 12, 13.

II. Association areas.
 1. Intermediate or border zones, with short fibers. 14, 16-33.
 2. Terminal or central zones, with long fibers. 34, 35-36.

The following is the list of zones, which is to be compared with the figures:

Areas Medullated Before Birth.

1. Lamina perforata anterior (trigonum olfactorium).
2. Upper third of the posterior central gyrus and the posterior surface of the corresponding part of the anterior central gyrus. Lobulus paracentralis.
2^{b}. Middle third of the posterior central gyrus.
3. Septum pellucidum with the diagonal Bandelette of Broca.
 Primary cingulum of Flechsig.
 Cortico-petal fibers of the fornix inferior.
4^{a}. Uncus (gyrus hippocampi) inner center for smell.
4^{b}. Subiculum cornu Ammonis.
5. Borders of the fissura calcarina.
 Polus occipitalis.
 Gyrus descendens.
 Lower third of the posterior central gyrus (2^{c} and 5^{b}).
6. Gyrus fornicatus, posterior half of the under surface, fornix longus.
7. Oblique gyrus of the gyrus temporalis superior.
7^{b}. (?) Upper half of the posterior gyrus of the island.
8. Part of the gyrus frontalis I.
8^{b}. Adjacent part of the gyrus fornicatus.
9. Upper part of the cuneus.
10. Inner surface of the polus temporalis.
11. Oblique gyrus of the pars triangularis of the gyrus frontalis inferior, outer part of the pars orbitalis.
12. Gyrus subangularis.

Areas Medullated After Birth.

13. Gyrus supra angularis.
14. Part of the gyrus temporalis superior.
15^{a}. Gyrus temporalis between 8^{b} and the genu corporis collosi.
15. Part of the gyrus frontalis superior adjacent to 8.
16. First parietal gyrus adjacent to 2.
17. Border of 5.
18. Foot of the gyrus frontalis medius.
18^{b}. Foot of the gyrus frontalis inferior.
19. Gyrus supra marginalis.
20^{1}. Anterior half of the third occipital gyrus.
21$_{2}$. Posterior half of the first parietal gyrus near 9.
22^{2}. Part of the island.
23$_{1}$. Gyrus occipito-temporalis.
24$_{1}$. Second occipital gyrus.
25. Gyrus fornicatus, a small portion beneath and behind.
26^{1}. Gyrus rectus adjacent to 11.
27. Middle part of the gyrus frontalis inferior.
28. Pole of the gyrus frontalis superior.
29. Rest of the gyrus supra marginalis.
30. Upper portion of the gyrus frontalis medialis.
31. Zone between the second occipital and second temporal gyri.
32. Under portion of the island.
33. Gyrus fornicatus near the præcuneus.
34. Gyrus angularis.
35. Inner surface of the gyrus frontalis superior, and the adjoining part of the gyrus fornicatus.
35^{b}. Gyrus frontalis II.
36. Temporalis II and III.

It is interesting to note that the first fibers to medullate in the brain are the primary sensory paths which extend from lower centers to the cortex. There are seven of these sensory areas on the cortex corresponding with the numbers 1, 2, 4, 5, 6, 7 and 8. No. 15 is a later extension of the primary zone 2, 2^{b}, 2^{c} and 8. Analyzing these seven zones we find that 1 and 4^{a} are primary olfactory areas connected by a band of medullated fibers with the olfactory bulb; 2, 2^{b}, 2^{c}, 8 and subsequently 15 represent the cortical zone for the sensory nerves of the skin and muscles, and have for subcenters the optic thalamus and globus pallidus; 5 is the area for sight and has its subcenter in the lateral geniculate body; 7 is for hearing and has its subcenter in the medial geniculate body, while 6 is possibly the primary sense area for taste and has its subcenter in the thalamus and globus pallidus. Thus these primary areas represent smell, touch, muscle sense, sight, taste and hearing.

The primary sensory areas have certain characteristics in common: (1) The first fibers to medullate in each one are the sensory paths from some subcenter. Later other fibers develop of the types of motor fibers, callosal fibers, arcuates and association bands, but each area has its own sequence in regard to these later systems. (2) The size of each area is proportional to the nerve or nerves supplying it, for example, the area for the skin and muscle nerves is the greatest, while the area for sight is greater than the area for hearing. (3) These primary zones can be definitely outlined in the early stages by the structure of the cortex. Moreover, the structure of the different areas is so characteristic that they can all be told apart. The structure of each area corresponds with the structure of its sense organ, for example, the many layers of the visual area correspond with the retina; the olfactory area has the fewest layers corresponding with the simple olfactory mucous membrane, while the islands of cells in the subiculum

cornu Ammonis, which are visible with the unaided eye possibly correspond with the taste buds. The area for hearing can be outlined macroscopically, for the cortex is twice as thick there as in the rest of the gyrus. The large central sensory area has a structure less characteristic corresponding with the simpler types of nerve endings. Thus each area is to be considered as a repetition in the cortex of a peripheral sense organ.

We will now take up in detail each sensory area. The first portion of the cortex to become medullated is the lamina perforata anterior (1) receiving fibers from the olfactory bulb. Later the olfactory fibers extend to the uncus (4). The cortex of these two areas is simple in structure and the medullated fibers penetrate the cortical layers. The olfactory system, which lies in the hippocampal zone, is the first to develop association bands. The first of these is numbered 3 in the list and is a band connecting the lamina perforata anterior with the globus pallidus by way of the septum pellucidum. A second band runs from the uncus through the subiculum to the cornu Ammonis. The Ammon's horn also receives an early bundle from the lamina perforata anterior by way of the inferior fornix (3). In a 9½ months' fœtus Flechsig found four bands of medullated fibers to Ammon's horn. The motor fibers of the system which begin in the large pyramidal cells of Ammon's horn and made the chief part of the fornix inferior, develop much later, 3 months after birth.

The great sensory area representing touch and muscle sense for the entire body begins to medullate next after the olfactory area. The structure of the cortex of this zone is less characteristic than the areas of special sense. But it contains in one part certain large sensory endings which Ramon y Cajal has shown are found nowhere else, while in another part it contains the characteristic giant pyramidal cells which give rise to the fibers of voluntary motion. It is the largest and most complex of the areas in regard to its primary sensory bands; that is, a number of sensory bands appear in the following order: 2, 2^b, 2^c and 5^b, then later 8, 8^b, 15 and 15^b. The sensory paths from the legs are the first to reach the cortex. They end in the paracentral lobule and in the upper third of the posterior central gyrus, extending on to the posterior surface of the corresponding anterior gyrus. The corresponding motor fibers develop from the area of the large pyramidal cells of the adjacent anterior central gyrus. Thus the sensory and motor areas are not mixed except in the sulcus. In contrast with the areas for smell, sight and hearing, the central sensory area develops motor fibers after the sensory ones. Moreover, each area develops the motor bands in the same sequence as the sensory. For example, the area 2 develops its motor fibers before 8 has medullated sensory fibers. The sequence of the types of fibers for this area is: (1) sensory, (2) motor, (3) callosal, (4) horizontal and arcuates, (5) association bands.

Flechsig has analyzed some of the sensory bands of this area, throwing much light on the relations of the basal ganglia. The following is the list of these bands: (a) Fibers from the globus pallidus to zone 2; (b) fibers from the ventro-lateral nucleus of the thalamus to zone 2; (c) a large band from the globus pallidus to zone 2; (d) fibers from the cup-shaped nucleus and center median of Luys to zone 2^b; (e) from the ventro-lateral nucleus of the thalamus to zone 2^c, and (f) from the dorso-lateral nucleus of the thalamus to zones 8 and 8^b.

The cortical area for sight (5) is around the fissura calcarina, the gyrus descendens and the occipital pole. The calcarine fissure is so deep that the area is much greater than appears. The structure of the cortex of this zone is so characteristic that the area can be sharply outlined. The association bands are late in developing, and the motor fibers run with the primary optic radiation. The primary optic radiation comes from the lateral geniculate body.

The cortical zone 6 may represent taste. It receives fibers from the thalamus in part near the pulvinar. Flechsig thinks that taste is also represented in the central sensory area. Zone 6 is connected with the subiculum cornu Ammonis and is much like it in structure.

The fibers for hearing are the first to become medullated in the temporal lobe. These fibers come from the medial geniculate body and end in a small portion of the gyrus temporalis I, not more than 1 to 2 gcm. in area. The next fibers to medullate are callosal and arcuate fibers. Possibly Türck's bundle, which develops later, is the motor path for the area analogous with the pyramidal tract.

Turning now to the second group of the primary areas, 9-13, none of these areas have projection fibers nor are they connected with the primary sense areas. Flechsig calls them automatic unknown centers. All but one, 13, develop before birth.

The group of association centers 14, 16-36 is full of interest. They all develop after birth and all begin with association bands. The division of this group into intermediate and terminal zones is both anatomical and physiological. Around each primary sensory area develops a border zone of association centers; moreover, generally speaking the earlier sensory areas receive the earlier border zones. These border zones receive their first fibers from the corresponding sensory area, and later develop other association bands. The border zone for the central sensory area is 16, 18, 18^b, 19, 22, 26, in which it will be noted that 16 corresponds with 2, 18 with 2^b, etc. The border zone for the optic area consists of 17, 20 and 24. Certain of the border zones are late in developing; for example, the one is the island of Riel, 32, and the præcunea 33, which may be the border zone for smell and taste.

The last three of the association centers 34, 35 and 36 do not develop in relation to any one primary sensory area, but rather they are in the center of a whole group of the border zones. 34 is the posterior association center, 35 the anterior or frontal area, and 36 the temporal. These centers are the last to develop and have long fibers.

Flechsig points out the enormous amount of work to be done in following the further development of the paths in the brain. The areas of the cortex do not stand out so sharply as the fiber bands become more complex, but even in

the adult it can be made out that the primary sensory areas have the most oblique and horizontal fibers, these being sensory conduction paths to other parts of the brain. The enormous numbers of fiber bundles in the adult, as well as the fact that many bundles turn abruptly in their course, makes it necessary to use pathological and special secondary degenerations as methods of research. The material is rare and the difficulties of obtaining it so great that only through coöperation between the members of the central committee and physicians and hospitals can we hope for great progress.

Flechsig takes up the results of the studies of degenerations and shows that the central sensory area as usually outlined is a mixture of true and false observations. The paths which degenerate from this central area are:

1. Cortico-spinal paths, the pyramidal tracts.
2. Cortico-bulbar paths, part in the lemniscus medialis.
3. Cortico-prontal paths, Arnold's bundle.
4. Cortico-thalamic paths (lateral nucleus).
5. Thalamo-cortical paths (ventro, lateral, central and cup-shaped nuclei).
6. Lenticular nucleus—cortico-paths.
7. Paths to the substantia nigra.
8. Cortico-quadrigeminal paths.
9. Paths of the red nucleus.
10. Paths of the nuclei of the posterior columns by way of the lemniscus medialis.

Of these 1-5 are proved for the human brain; 9 and 10 degenerate indirectly. Beside these fibers callosal and association bands degenerate. None of the pyramidal tract fibers arise in the posterior central gyrus, but rather in the lobulus paracentralis and the two upper thirds of the anterior central gyrus. The motor fibers from the lower third of the anterior central gyrus, the zone of the cranial nerves, run with the lemniscus medialis.

The fibers from the cortex to the pons and medulla (2 and 3) are not well known. They lie internal to pyramidal fibers in the pes. There are numerous bands connecting the optic thalamus and the cortex, 4 and 5. Through analyzing the degenerations, Flechsig confirms the points brought out in development, namely, that the sensory fibers end in the posterior and the motor fibers begin in the anterior central gyrus. The parietal lobe area (16) does not give degenerating projection fibers. The globus pallidus shows but few fibers which degenerate from the cortex, but the substantia nigra has many.

The study of degeneration of the optic area confirms the evidence of development. The primary optic radiation (Flechsig) which runs in the area of Vicq d'Azyrs' stripe degenerates upward from the lateral geniculate body and pulvinar to the occipital cortex. The fibers that degenerate downwards lie next the callosal fibers. In this connection Sherrington and Grünbaum's experiments on apes are most interesting, for they showed that stimulation in the region of Vicq d'Azyrs' stripe causes movement of the eye muscles; that is to say, the motor path for the eye muscles comes from the optic center of the cortex, just as the pyramidal tract starts near its corresponding sensory center. No projection fibers degenerate from 17, 17^b, 20 and 9.

The errors in regard to degeneration from the temporal lobe are due to not analyzing its different portions. Türck's bundle connects only with zone 7. It has two bundles of fibers ascending and descending and they come from different parts of the zone:

The results of degenerations in the association areas are complicated and unsatisfactory.

Flechsig now takes up the question of the relation of the motor and sensory fibers in each zone. He suggests the name of projection fields for the seven primary zones. The motor and sensory bands for each projection zone are as follows: 1. The olfactory projection zone has bands from the tractus olfactorius to the lamina perforata anterior and the uncus and descending fibers to the globus pallidus and to the ganglion habenulæ by means of the tænia thalami optici. 2. The central projection zone is the end station (indirect) of the lemniscus medialis and the superior cerebellar peduncle and the origin of the pyramidal tract for the cord and Arnold's bundle for the pons and medulla. 3. The uncus and gyrus hippocampus have several cortico-petal paths from the olfactory tracts and internal capsule and a motor path in the inferior fornix. Field 6 has an early sensory path from the internal capsule, and a later one from the thalamus. The optic area receives sensory fibers from the lateral geniculate body and thalamus and sends motor fibers to the superior quadrigeminal body. The sensory fibers of the ear path come from the medial geniculate body and the motor fibers run in Türck's bundle. The rest of the cortex is without projection fibers and if one considers the optic thalamus all parts of it have been related to the projection areas—the upper part of the thalamus to the central, the posterior to the visual, a part of the posterior and inner zone to hippocampal zone and the frontal part to the central zone and hippocampus.

The relation of the sensory and motor fibers within the projection fields is known only for the central field. The convincing experiments of Sherrington on the gorilla are confirmed in man by the myelinization. Sherrington found by careful stimulation of the cortex and subsequent extirpation of the areas that the motor fibers come from the anterior central gyrus only and not the posterior. This relation for the other zones is as yet unknown.

In connection with aphasia, Flechsig shows that Broca's field is a complex of several zones, and Wernicke's area corresponds with Flechsig's primary hearing center. The existence of complicated centers for the various phases of spoken and written language, as well as word memory, is unquestioned and there are probably multiple centers in the zones of 16-36, indeed probably a considerable part of the zones 16-36 are associated with these complicated phenomena, but to definitely locate these areas on theoretical grounds without basis of fact hinders rather than helps the development of our knowledge.

A general view of this work of Flechsig's shows that in the brain there are primarily projection centers which are the

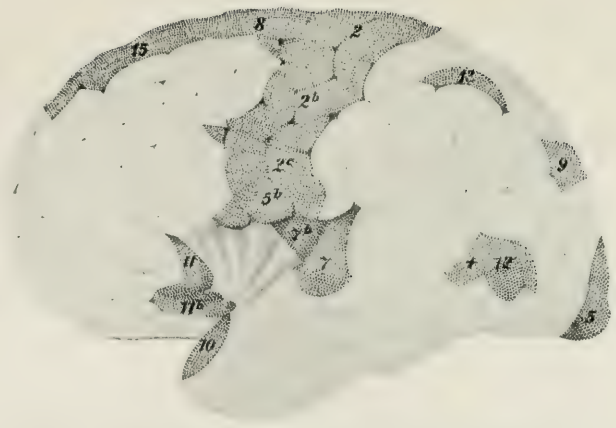


FIG. 1.—LATERAL SURFACE OF THE BRAIN SHOWING THE PRIMORDIAL AREAS, BOTH SENSORY AND AUTOMATIC, IN DOTTED ZONES.



FIG. 3.—LATERAL SURFACES OF THE BRAIN SHOWING THE PRIMORDIAL AND MARGINAL ZONES.

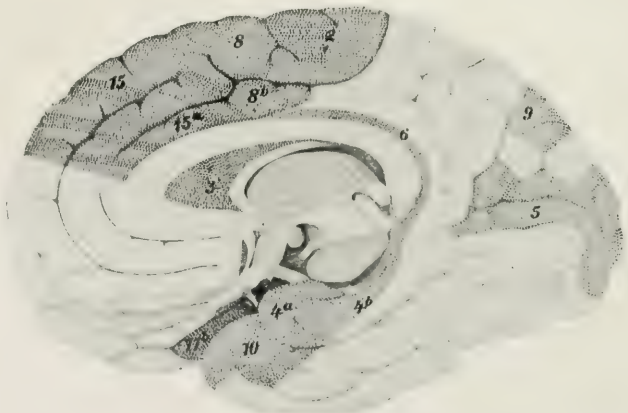


FIG. 2.—SAME ZONES ON THE MEDIAL SURFACE OF THE BRAIN.

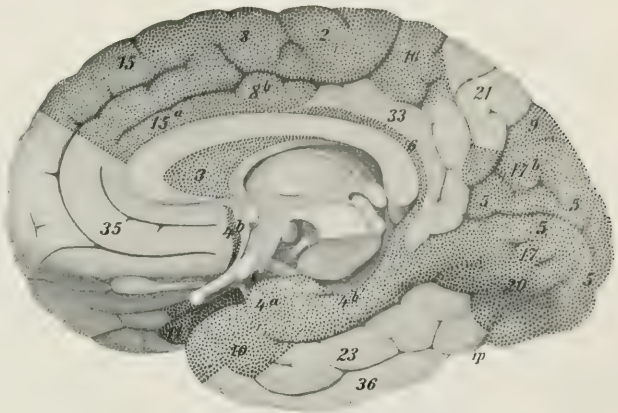


FIG. 4.—SAME AREAS ON THE MESIAL SURFACE.

areas which represent the various sensory paths and their corresponding motor tracts. They are the first to medullate, the first to develop, the first to have callosal fibers and the first to send association bands to other parts of the brain—so they are in all respects primary and fundamental. There next develop a few automatic centers of unknown meaning. The third step consists in laying down a marginal zone of association centers around each primary projection center. Each center has a group of these which develop in the same sequence as the corresponding primary center. Certain of these association areas are closely related to one projection center; for example, 16 is related to 2, but others, as for example the gyrus angularis, represent several projection centers, sight, hearing and taste, for its destruction causes a disturbance of all three of these senses. The primary projection centers are not directly connected with others; for example, no fibers run from the optic to the hearing center, etc., and the connections are made wholly through the association zones 16-36. Finally, the great association centers 34-36 are not independent isolated areas, for the great anterior association area stands in close relation to the central projection area representing the body and in slight relation to the olfactory area, while the others are more closely related to the areas of special sense.

Flechsig closes this inspiring work with some suggestions for the work of the future, the outlook for which he has made brilliant and possible. There is the field of the early development, begun by His, before medullation begins; then the whole subject of the development of the association bands. The primary relations of the fundamental association bands in their relation to the primary association centers can all be worked out on animals, perhaps especially well in the lower vertebrates. Flechsig ends with the suggestion that the whole gross anatomy of the cortex for which we have now but the outline of markings which are not fundamental, as for example the sulcus of Rolando, can now be reworked in the light of our new knowledge.

A NOTE ON THE DEVELOPMENTAL RELATIONS OF THE KIDNEY AND URETER IN HUMAN EMBRYOS.

BY AUGUSTUS G. POHLMAN, M. D.,

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The first signs of the permanent kidney (metanephros) is found in a dorsal outgrowth of the Wolffian duct close to its orifice in the cloaca. The Wolffian duct (segmental) reaches the caudal part of the enteron in embryo 76[1] (4.5 mm.). It is of even caliber throughout its course, dilating slightly as it enters the cloaca. As the duct comes into relation with the cloaca, two varieties of epithelium meet, the mesodermic epithelium of the duct and the entodermic of the gut. There must of necessity be an epithelial plate separating the duct from the cloaca, but it probably disappears with its formation.

In the slightly older embryo 80 (5.0 mm.) the duct has given off a small shoot which arises dorsally and continues the lumen of the duct into the mesodermic tissue as yet undifferentiated, in which the whole is embedded. The lumen of this bud, the renal bud, is somewhat larger than that of the duct proper and is dilated toward its blind end. The surrounding tissue has become condensed about the end of the bud and is easily recognized by its different arrangement and by its darker stain with carmine. The renal anlage is placed at the second sacral vertebra as nearly as can be estimated, in the uncertainty of the vertebræ at this stage and the difficulty in fixing the direction which might be called the right angle to the bent vertebral column. This position does not change until an older stage is reached as was verified in the models of embryo 2 (7.0 mm.) by Professor Mall and embryo 163 (9.0 mm.) by Professor Bardeen.

The renal anlage may be divided into two distinct parts in embryo 2 (7.0 mm.); a segment not surrounded by specialized mesodermic tissue, the future ureter, and a segment capped by the specialized tissue, the renal mesenchyme, the kidney and all the derivatives of the bud included within the kidney substance. The two anlages, the right and left, point dorsally from their position on the Wolffian ducts and even converge toward the middle line, and approach each other so closely that it is a matter of 50 microns separating them. The buds are at the same level and the ureter and kidney segments are of equal size.

In embryo 88 (9.0 mm.) the distal end of the bud undergoes a division into an upper and lower sprout which are enclosed in the renal mesenchyme and represent the future upper and lower pelves of the adult kidney. The renal mesenchyme in the meantime has developed in a vertical direction and is bean-shaped. Stationary up to this stage the kidney now begins a rapid wandering to its future permanent position in the body.

The sharp division into an upper and lower sprout is lost in embryo 114 (10.0 mm.). The renal mass is distinctly bean-shaped in reconstruction and rather flattened from side to side. The hilum is situated ventrally. The ureter has elongated but is still in relation with the Wolffian duct dor-

[1] This and other similar figures refer to the catalogue number in the Anatomical Collection of the Johns Hopkins Medical School.

sally. The kidneys are placed with their upper ends at the brim of the pelvis, the one a little higher than the other. The hilum of the kidney is well marked although the organ is as yet not vascularized. The two kidneys are placed with their long axes parallel and measure from tip to tip about 0.6 mm. and are about 0.2 mm. apart.

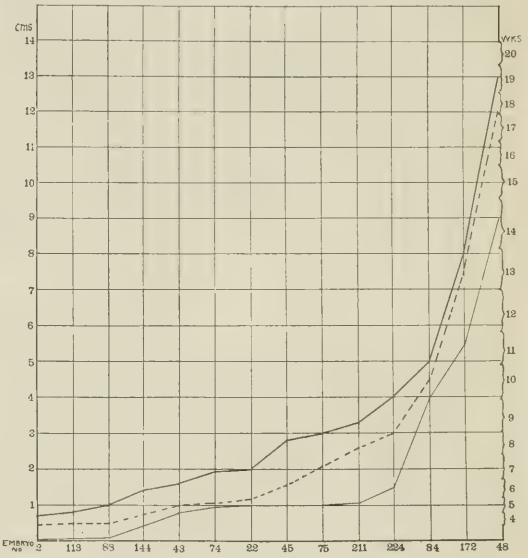
The upper border of the developing kidney reaches the third lumbar vertebra in embryo 144 (14.0 mm.). The ureter still emerges from its ventral aspect, but the relations at the lower end have changed. The ureter is rotated to a lateral position on the Wolffian duct and that portion of the duct which lay between the bud and the cloaca has disappeared (?), bringing the orifice of the ureter directly at the cloaca or into the duct at the cloaca. The kidney is without blood supply and lies behind the Wolffian body.

In embryo 43 (16.0 mm.) the kidney lies higher than in the preceding embryo. In addition it has undergone an axial rotation bringing the hilum to its mesial border, i. e., turned about 90° toward the middle line. The ureter has acquired a distinct orifice into the ventral segment of the cloaca lateral to the orifice of the Wolffian duct. The cloaca is completely divided at this stage.

The kidney arrives at its normal height in embryo 22 (20.0 mm.). The rotation is maintained and the kidneys, except that they lie closely together, are in the adult position. The vascularity is as yet problematic. In the meantime the ureter has lost all connection with the Wolffian duct and has grown into a higher and more lateral location as a fixed structure. The Müllerian ducts in this embryo are unusual in that the left duct has reached the urogenital sinus while the right lies a full slide higher up. The kidneys are about 1.0 mm. apart.

Chronologically: The Wolffian duct joins the cloaca at 4.5 mm.; the renal buds appear at 5.0 mm.; the renal buds may be differentiated into two segments, the ureter and kidney, at 7.0 mm. when they lie opposite the second sacral vertebra; at 10.0 mm. the upper border of the kidney is at the brim of the pelvis; at 14.0 mm. the ureter lies lateral to the Wolffian duct and the upper pole of the kidney is at the third lumbar vertebra; at 16.0 mm. the kidney has passed the midlumbar line and has been rotated through 90° on its long axis while the ureter has a separate orifice in the urogenital sinus; at 20.0 mm. the ureter and kidney are in the relative normal position and the Müllerian ducts have gained the sinus.

The rotation of the kidney and the displacement of the ureter at the lower end, although they occur at the same time, are distinct processes. This may be demonstrated in cases of incomplete double ureter where the ureter is divided into two segments somewhere along its course. The ventral segment proceeds from the upper pelvis of the kidney, while the dorsal branch is connected with the lower pelvis. If there were any connection between the rotation of the kidney at the midlumbar line with the lateral displacement at the lower end of the ureter, there would be evidences of such rotation along the course of the anomalous branches of the ureter, but we find the position of the two segments, the one ventral to the other maintained even in the adult with no manifestations of any rotation in an embryo with similar malformation. Comparing this variation with cases of complete reduplication of the ureter we find the relation of the two segments the same, one ventral to the other, although there is displacement of the ventral ureter in that its orifice lies between that of the dorsal ureter and the Wolffian duct. This crossing of the two ureters is only found at the lower end and does not affect the course of the ureter above. Again in all cases where there is congenital displacement of the kidney and lack of rotation or mal-rotation, the orifice of the ureter is not necessarily affected and in those cases in which the ureter is widely displaced in the female through downgrowth of the Müllerian



ducts, the kidney position and ureter course are normal otherwise.

In the accompanying chart are found curves to represent the wandering of the kidneys; the age in weeks is shown on the right, the size in centimeters on the left, and the number of the embryo plotted below. The uppermost curve is derived from the vertex-breech measurement of the embryos in question, the second and dotted curve the size of the kidney from tip to tip multiplied 10 times, the lowest curve the distance between the two kidneys also multiplied by 10. The kidney does not grow as rapidly as the body up to embryo 22 and then gains on the body size until at 130 mm., the kidney is about 1-10th the vertex-breech measurement. The distance between the kidneys remains practically the same until 88, then grows apart rapidly (the period of wandering) until 74 is gained when it remains about the same until 224 although the difference between these two embryos, 74 and 224, is 21.0 mm., or in time, about ten days. The kidneys

then grow apart even more rapidly than during the period of wandering. This quiescent time I hold to be the stage of vascularization.

It was stated in an earlier part of this article that the kidney is not vascularized until it has reached its normal height, and that it attains this position in an embryo of about 20.0 mm. This corresponds to the curve. Mr. Eben C. Hill of Johns Hopkins University has also verified this matter in the pig and the fact that the renal artery may sometimes give off the suprarenal and spermatic strengthens the point made.

The idea that the primitive upper and lower sprout of the bud correspond to the upper and lower pelves of the adult kidney is entirely compatible with the findings in the embryo and the adult. My report on the complete doubling of the ureters in embryos, Mall 172 and Keibel-Piper have confirmed the same in the most important stages in the embryology of this form of anomaly. The form of the pelvis and ureter is undoubtedly dependent on the development of the renal bud while the kidney form is controlled by the mesenchyme.

I wish in closing to express my indebtedness to Professor Mall for the use of all the numbered embryos and of his model of embryo 2, to Professor Bardeen for the loan of his models of embryos 163 and 144, to Professor Keibel for embryo Keibel-Piper and to Mr. Hill for data of his findings in the pig.

ABNORMALITIES IN THE FORM OF THE KIDNEY AND URETER DEPENDENT ON THE DEVELOPMENT OF THE RENAL BUD.

By Augustus G. Pohlman, M. D.,

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The vague references to the embryology made in the usual reports of renal variations are possibly a result of the anatomist not interesting himself sufficiently in what might be termed "abnormal variations." The cases are written up by the clinicians, who necessarily orient themselves as to the development of the tract from the text-books, as no scheme has as yet been worked out to which he may refer in his attempt to classify or account for the interesting and important anomalies of the kidney and ureter. Even the excellent papers of Bachhammer and of Schwarz are lamentably hidden by the obscurity of their titles.

Cases of renal malformation are comparatively rare, but they occur frequently enough to be of interest to the clinician as well as to the anatomist and pathologist. I need only mention the cases of single or misplaced kidney; to the removal of a single unilateral kidney or to the obstruction of the pelvic inlet by a misplaced organ, to illustrate the importance of a thorough knowledge of the anomalies of the urinary tract. It naturally falls upon the shoulders of the anatomist to classify variations, and as these abnormalities are usually the result of faulty development, the basis of the classification must be an embryologic one. That such a classification will include all the anomalies is quite out of the question at present. There will always be a few which cannot be explained, but the number will grow proportionately less as our knowledge of embryology advances. Before the development of the kidney and ureter had been worked out, speculations regarding the origin of abnormalities were far removed from the present accepted ideas.

The first great difficulty met with in the classification of variations from a developmental standpoint is to make the system clear and embracing, and to present the matter in such a form that it may be of use to someone beside the writer. This scheme must be based on facts in the embryology which have been verified personally, and the possible results compared with actual cases. Here again an element of error is met with in that many of the reports are crude and superficial, and too much credence must not be given to them. The exceptions are surprisingly few, and in the field covered in this paper are limited practically to one observer.

The literature referred to is necessarily small, as it was not deemed advisable to conceal any merit the classification might possess by involved references and case citings. Only those anomalies will be considered where both kidneys are present. This subject is excellently covered in the articles by Ballowitz, Moore and Morris, and the possible causes mentioned in my paper in "American Medicine."

I am obliged to set another limit to this paper in that I shall consider only those anomalies which have their origin before the third month. This excludes all congenital abnormalities which depend on the excretory function of the kidney for their manifestation—congenital cystic kidney, congenital hydronephrosis, etc., also the minor variations which are of relatively little importance, as persistent lobulation, etc. In the variations to be mentioned, the kidney is quite normal excepting in its form, and in the form of the pelvis and ureter.

The development of the renal bud has been thoroughly worked out. I will mention the article by Keibel on its earlier stages and that by Hauch on its later development. My own findings have been a confirmation of what has already been demonstrated by many investigators. I will review the embryology of the kidney and ureter by referring to the conditions present in embryos chosen from the Mall collection, from the earliest stage in the development of the tract to an age in which the kidney and ureter have assumed their relatively normal shape and position. The embryos are arranged according to their size, but the figures do not correspond exactly to those mentioned in other articles. It will be remem-

bered that all embryos of the same age are not always of the same size, and allowance must also be made for shrinkage in fixation and embedding.

The embryos are normal and in perfect series. The relations of the kidney and ureter were not only studied from the sections but modeled as well. The review presents the general development of the tract concisely and in sufficient detail for the objects of this article.

In embryo Mall 164 (3.5 mm.) the cloaca is relatively spacious. The Wolffian duct has not yet reached it and the stage is therefore too young for a study of the urinary tract.

The Wolffian ducts reach the cloaca in a trifle older stage, embryo Mall 76 (4.5 mm.), and empty well to the front in the lateral wall. There are no signs of the development of the renal buds.

The renal buds appear dorsally on the Wolffian ducts (embryo Mall 80—5.0 mm.). They arise near the cloaca and their blind ends are already capped with renal mesenchyme developed from the surrounding undifferentiated mesodermic tissue.

In embryo Mall 2 (7.0 mm.) the buds have elongated markedly and the cap of renal mesenchyme to each bud is more distinct and confined to the distal and blindly ending part. One may already separate the developing tract into two segments; the one surrounded by mesenchyme, the kidney; the other from a portion which is not, the ureter. The blind end of the bud shows no signs of dividing. The masses of mesenchyme are placed at the level of the second sacral vertebra.

The blind end of the bud shows the first signs of sprouting into an upper and lower division in embryo Mall 163 (9.0 mm.). The splitting occurs within the mesenchyme which has increased in size particularly in the vertical diameter.

The definiteness of the upper and lower division is lost in a slightly older stage, embryo Mall 114 (10.0 mm.), and the condition may more properly be spoken of as a common pelvis to the developing kidney. The two masses of mesenchyme have already assumed the typical bean shape and lie close together with their long axes parallel. The ureter emerges ventrally from each but is still dorsally placed on the Wolffian duct, although the segment of the duct between the cloaca and the ureter has shortened. The upper border of the kidney is at the brim of the pelvis.

Embryo Mall 144 (14.0 mm.). The kidney lies opposite the third lumbar vertebra and has begun an axial rotation, bringing the hilum toward the middle line. The ureter has also assumed a lateral position on the duct, and the segment of the duct between the ureter and the cloaca has practically disappeared. It may be said that the ureter has a distinct orifice into the urogenital sinus (ventral segment of the cloaca).

In embryo Mall 43 (16.0 mm.) the ureter has an orifice lateral to the Wolffian duct. The kidney is completely rotated and the hila point toward each other. The upper border of the kidney is opposite the first lumbar vertebra.

The kidney reaches its normal height about the end of the second month and then receives its blood supply, the vascularization coming directly from the aorta and occasionally from the suprarenal artery. The vessels seem to choose the nearest route and go to the hilum, the branch from the suprarenal sometimes entering the upper pole.

The ureter grows away from the Wolffian duct, embryo Mall 22 (20.0 mm.) and empties higher and more laterally. Keibel describes a trigone in his embryo Lo (24.0 mm.). The ureter assumes its relatively normal position in the same stage in which the kidney reaches its normal height or about the end of the second month. The two processes are, however, quite distinct. The change in the position of the kidney is due to the development of the distal part of the bud and its surroundings, while the change in the position of the ureter is related to the growth at the lower end of the Wolffian duct. It is interesting to note that the ureter normally loses its connection with the Wolffian duct before the Müllerian duct reaches the urogenital sinus.

The earlier development of the renal bud may be represented by three simple figures upon which the diagrams used in the later discussion of the variations will be based. Figure 1 represents the first budding from the dorsal side of the Wolffian duct at a short distance from the cloaca; Figure 2, the first subdivision of the bud within the renal mesenchyme (stage of embryo Mall 163); and Figure 3 shows Figure 1 (stage of embryo Mall 2) viewed from above. The figures are schematic, but give a fair idea of the relations found in the models of these embryos.

I take the liberty of repeating the tabulation of the steps in the development of the tract as published in "American Medicine:"

I. The renal bud arises dorsally on the Wolffian duct after the duct has reached the cloaca and at a short distance from its entrance.

II. The two buds grow dorsally, lying close together, each being capped with a mass of renal mesenchyme.

III. Each bud divides into an upper and lower sprout at some distance from the Wolffian ducts.

IV. The kidney wanders upward from a position in front of the second sacral vertebra, rotates at the midlumbar region, and finally reaches its normal height about the end of the second month.

V. It becomes vascularized after it has reached its normal height.

VI. The ureter changes its position on the Wolffian duct from dorsal to lateral and comes to empty distinct from it.

VII. The ureter loses its relation to the duct entirely and opens higher and more laterally.

It may appear that something is taken for granted when it is assumed that the upper and lower sprout of the renal bud found in an embryo of 9.0 mm. are represented in the adult by the upper and lower pelves of the kidney, especially when the division into an upper and lower sprout is replaced in an older stage by a "common pelvis." However, the assumption is a fair one: there are two sprouts, an upper and a lower, and correspondingly two pelves; in doubling of the

ureter the ventral ureter always arises from the upper pelvis as would be expected from the development; and finally, this assumption makes it easy to account for the anomalies to be considered later.

This idea that the upper and lower pelves of the kidney are determined in the earlier stages of its embryology, is contrary to the views held by some that the division of the pelvis into an upper and lower segment is due to the development of the renal parenchyma. The formation of the kidney parenchyma is secondary to the development of the ureter and its derivatives, and the idea that the growth of the kidney mechanically divides the pelvis is not substantiated in the formation of the anomalies nor does it even allow for the persistence of the lobulation normally present in the beef kidney.

It is granted in this article that the kidney is derived from a double anlage, the renal mesenchyme directly dependent on the renal bud, and that the division into an upper and lower pelvis is determined in the early embryology. It is upon these assumptions that I have based a scheme to be followed in the classification of anomalies of the tract.

No one has observed these variations at the time they were forming, and hence the scheme is merely a hypothesis. However, granting that certain changes do occur normally, is not a hypothesis that will account for the variations from this normal, and simplify the complex embryology of the developmental faults, better than no system whatever? Many renal variations are so rare that it is doubtful whether they will ever be observed in the earlier stages. Even some of the more frequent anomalies as doubling of the ureter has been reported but once in young embryos (Soulié). It was my good fortune to find two cases of complete double ureter in two embryos under the third month. One was discovered quite accidentally, and the other was found in working through the Mall collection. Two cases in over sixty embryos studied.

In all the anomalies to be mentioned none are directly pathologic because all the subjects attained an old age or died from causes quite apart from an abnormal kidney. This is no more than natural, for if the kidneys were not normal at birth, the chances for the individual reaching the age of puberty would be small. The variations are therefore only of interest from an anatomic point of view and indirectly of importance to the surgeon. The malpositions of the kidney have a greater interest to the clinician and it is my purpose to present that side of the subject at some later date. The clinical aspect is dealt with in a very thorough manner by Morris.

Anomalies of the kidney may be unilateral or bilateral, and for convenience sake the paper may be divided into three sub-headings:

A. Changes in form of the ureter.

B. Changes in form of one kidney.

C. Changes in form involving both kidneys.

Changes in form of the ureter may be present in changes in form of the kidney or they may be found in normal kidneys. The abnormalities of the ureter are dependent on the renal bud, while the anomalous kidneys result from an abnormal development of the renal mesenchyme, again influenced by the renal bud. The term abnormal refers merely to form and not to function.

A. Variations in the Form of the Ureter and Pelvis.

A 1. *Incomplete Double Ureter.*

Should the renal bud divide too early, or the division extend into the ureter segment (see Fig. A 1), that splitting found in the ureter itself would remain a permanent one and any variation might exist as a result from an exaggeration of the usual upper and lower pelves to an incomplete reduplication of the ureter. An incomplete double ureter may be defined as two ureters with a common orifice.

The more complete the division of the ureter segment, the more complete the reduplication. The pelves of the kidney would always be distinct, and it is fair to assume that each subpelvis would follow the rule for the usual normal, and divide into an upper and lower segment (to be dealt with later under A 4).

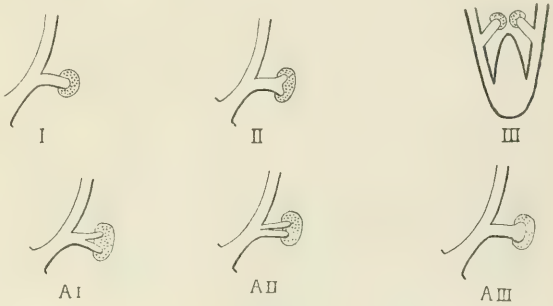


FIG. A.

The ureter from the upper pelvis will normally lie ventral to the ureter from the lower one, as will be evident from the diagram. There are exceptions to this which have a slightly different origin and these will be considered under B 2.

Cases of incomplete double ureter are the most frequent of all renal variations, and are met with yearly in almost every dissecting room. I refer the reader to the article of Schwarz, p. 172, for a review of a number of reported cases, and also to the figures in the paper of Hauch.

The rule for incomplete double ureter may be stated as follows: The pelves of the kidney are always distinct, the ventral ureter arises from the upper pelvis and there is one orifice which is usually normally placed. It is important to distinguish the incomplete double ureter from the complete variety, and in the report of cases the distinction is not often made. Fig. A 1 of the plate represents a very common type of this anomaly.

A 2. *Complete Double Ureter.*

Should the splitting of the renal bud be so complete that it is affected by the shortening of the segment of the Wolffian

duct lying between it and the cloaca, it is possible for each division to acquire a distinct orifice in the duct as is shown in Fig. A 2. This would result in complete double ureter.

The explanation seems a more likely one as the complete double ureter conforms to the rules laid down for the incomplete variety. The only differences are found at the bladder end because of the two distinct orifices.

Cases of complete double ureter are rare but the anomaly has been reported quite frequently in the adult. It was my good fortune to discover two cases in embryos under two months old; one in embryo Piper, the property of Professor Franz Keibel under whom I began to study the development of the human urogenital system, and the other, embryo 175 of Professor Mall's collection. I am indebted to both Professor Keibel and to Professor Mall for the loan of the embryos mentioned in this paper, and also to Mr. Max Broedel for extremely useful suggestions regarding the anomalies of the kidney, and the privilege of mentioning one of his own cases.

Embryo Mall 175 (13.0 mm.). This embryo is cut at twenty microns and stained in carmine. It is well preserved and entirely normal. The sex from the histology of the sex gland is male. The epithelium at the urogenital sinus is loosened a little but not sufficiently to interfere with the conformation. A model of the lower ends of the ureters and of the Wolffian duct was made X 50.

The left kidney and ureter are entirely normal. On the right side, the kidney is also normal but the ureter is completely double. The ureter from the upper pelvis is a trifle smaller and lies ventrally to the ureter from the lower pelvis. This relation is maintained until the ureters approach the Wolffian duct when the dorsal ureter swings laterally. The relation at the urogenital sinus from the midline is: Wolffian duct, ventral ureter and dorsal ureter.

As to the openings in the sinus, it is extremely difficult to say whether all three have a common orifice, or the ureters an orifice distinct from the Wolffian duct, or all three have separate openings. If the usually conceded fate of the lower part of the Wolffian duct is accepted—that it "unfolds" and enters into the formation of the bladder—any one of these possibilities may be held to be the correct one. Personally, I consider the case one of complete reduplication at a stage in which the lateral orifice is just beginning to shift to a higher and more lateral position.

Suffice it to say, that the two ureters change their relation as they approach the urogenital sinus, and that the dorsal ureter (the one from the lower part of the kidney) comes to lie lateral to the ventral ureter. This would probably be the same if the doubling were complete or nearly complete.

It will be noted that the change in position of the ureter from dorsal to lateral is at about the same time that the kidney undergoes axial rotation. Should the processes connected with the change in relation of ureter from a dorsal to a lateral position on the Wolffian duct be in any way connected with the rotation, the place of the crossing of the ureters would not be found at the lower end, and in cases where the kidney does not reach a normal height, where no rotation has taken place, the ureter would be abnormally situated—which is not the case. For these reasons, it is best to ascribe the changes in the position of the ureter to a development of the lower end of the tract and perhaps to the Wolffian duct as well.

Embryo Piper-Keibel (24.0 mm.). The same condition is found at a later stage in the development. The embryo was cut at fifteen microns and also stained in carmine. The sex is male. On the right side, there is a complete double ureter with two well defined orifices in the bladder. The ureters hold the same relation as that described in the Mall embryo and the ventral ureter swings mesial to the dorsal one as they approach the urogenital sinus. Owing to the development of the bladder, the lateral ureter opens higher and more laterally. It was found to lie in the normal position on comparison with the orifice on the other side. The ventral ureter was probably placed in a position of disadvantage for it lay in the path of the resultant of the forces —between the lateral ureter and the Wolffian duct.

I find a reference in an article by Weigert where in speaking about complete double ureter, he says: "In allen Fällen entsprach die tiefere liegende Öffnung in der Blase dem Ureter, der vom oberen Nierenbecken kam, die andere dem, der vom unteren entsprang." This agrees perfectly with my findings in the embryos and with the cases cited in the literature, with a single exception. This is a case reported by Hudson, who pictures a specimen of complete double ureter in which the ventral ureter empties higher than the one from the lower part of the kidney. The specimen was drawn after removal from the body, and it would be a most natural proceeding to uncross the ureters.

There is also an exception to the rule that the more ventral ureter comes to lie mesial to the more dorsally placed one, for according to Weigert: "In den anderen vier Fällen fand eine vollkommene Kreuzung statt, indem der vom oberen Nierenbecken kommende Ureter, der bis dahin medial vom anderen Lag, nunmehr an dessen vordere und laterale Seite zu liegen kam, und in dieser Lagerung bis an die Blase hinanging. Nach der Kreuzung und namentlich in der Nähe der Blase lagen die Ureter sehr dicht bei einander."

Exactly how this is meant is not quite clear to me. It is quite impossible to account for the condition in which the mesial ureter comes to open higher, and I am tempted to await other cases before giving up the idea that the ureter with the higher orifice must lie lateral to the more mesial opening. In a case reported by Hyrtl the orifices are described as lying side by side.

In one of Weigert's cases, he mentions the relation of the ureter from the lower pelvis as lateral to the one from the upper part of the kidney. The case is also pictured after the removal of the organs from the body and would be quite possible. The other two exceptions will be explained under B 3.

The rule for complete double ureter may be stated: that the relations of the two ureters and pelvis are the same as in incomplete reduplication, and the ureter from the upper

pelvis has the lower orifice in the bladder and lies somewhere between the higher opening of the dorsal ureter and the opening of the genital duct. The literature is reviewed by Schwarz, p. 175, and a report of twelve cases is found in the article by Weigert. The doubling according to the latter is usually on one side only.

A 3. *Common Pelvis.*

Should the division of the renal bud into an upper and lower sprout be suppressed, or should the later stage of common pelvis persist, there would be no involvement of the ureter and the form of the pelvis would not affect the shape of the kidney because that organ would have its normal origin—from one mass of renal mesenchyme. I find such cases cited by Hauch: "Man sieht die dicken plumpen Formen (casts of the pelvis), die sich garnicht in Calyces teilen, sondern einen leicht konvexen ausseren Rand haben, an welche sie die Fornices fast ohne Calyxbildung aufnehmen" Fig. 31, 32.

This must be considered a persistence of the stage of common pelvis. It is also found in pathologic conditions, and is, according to Broedel, the first sign of a beginning hydronephrosis which mechanically transforms the upper and lower pelvis into a single one. This is entirely in keeping with the view that the division is due to the development of the cortex. That the damming back of the urine may have this effect is perfectly possible, but that the condition mentioned by Hauch is a variation in the development, is also a fact.

The variation is but a slight one and has no clinical importance or particular anatomic significance.

A 4. *Multiple Pelves and Ureters.*

The sprouting of the renal bud takes place at the upper and lower poles and the question naturally arises, in case there are two pelves, the one above the other as is normal, does each pelvis divide into an upper and lower subpelvis as is the rule for the adult form? If we represent the state of affairs in a stage corresponding to an embryo 9 mm. long by a subdivision of the anlage for a doubling of the ureter, one sprout might divide and the other not as shown in Fig. A 4 a., or both might divide as in A 4 b.

In the former condition the lower pelvis would show the normal division in a kidney with complete or incomplete double ureter and two pelves, the upper simple and the lower divided. This I hold to be very uncommon, and know of no case. In the article by Hauch (Fig. 78) there is illustrated the cast of the upper part of the ureter and pelvis of a kidney in which the double subdivision is clearly shown.

The form of the kidney, if it has been developed from one mass of renal mesenchyme, is not affected by abnormalities of the pelvis, and in this I agree with Hauch: "Diese äussere Form der Niere hat keine oder nur sehr wenig Bedeutung für die Form des Nierenbeckens; ich verglich die Ausgüsse der verschiedenen, oben besprochenen Nieren mit den Abbildungen von deren Ausseren und sah, wie alle die verschiedenen Formen der Pelvis von des äusseren Form der Niere *durchaus unabhängig* sind."

The doubling of the ureter is always in one plane and the parts are arranged from above down. In case an exaggeration of the condition represented in Fig. A 4 b. be found in the adult, it would correspond to the description of that of Richmond, in which there were four divisions to the pelvis. Four distinct ducts led from either kidney, and at a point some four inches below the hilum, united into a common pelvis and afterwards were replaced by a normal ureter with normal opening in the bladder. Although the fact was not mentioned, it may be taken for granted that the pelves were distinct and that the rule for incomplete double ureter held. The division in such a marked manner is extremely rare and may be counted the least common of the variations in the form of the ureter.

The anomalies thus far discussed only affect the form of the ureter, and as has been seen, are determined in the early development of the renal bud. All these variations may be present in abnormalities in the form of the kidney with the exception of the common pelvis. In all marked congenital variations in the form of one kidney the ureter is either completely or incompletely doubled.

B. Variations in the Form of one Kidney.

It is of course understood, that the kidney form varies to some extent as it is moulded more or less to fit in its surroundings, and that these minor differences are not included in the scope of this article. Only those anomalies are to be considered which are directly dependent upon the development of the renal bud and mesenchyme. It was mentioned that as long as the kidney was developed from one secondary anlage, its form would be normal no matter what the abnormality of the ureter. It must be inferred therefore that the kidney may be derived from more than one secondary anlage if anomalies in the form are found.

Should the sprouting of the renal bud begin early, or the division be placed at different points, or the sprouts be more divergent than is usual, each division might stimulate a mass of mesenchyme, and there would be a *double* secondary anlage for the kidney. These anlages are naturally placed one above the other and might remain distinct as shown in Fig. B 1, or might fuse at an earlier or later date as represented in Fig. B 2.

Granting the condition in B 1 persistent, there would be complete doubling of the kidney, two distinct kidneys on one side with complete or incomplete double ureter, and whether the ureter be completely or incompletely double, the form of the kidney would be the same.

B 1. *Free Supernumerary Kidneys.*

A case is reported by Thielmann which gives an excellent illustration of doubling of the kidney with incomplete double ureter. The anomaly is described in great detail and I present the essentials which concern us.

The left kidney was normal but a trifle large. The right kidney was smaller but also normally formed and placed. The third kidney was situated upon the right common iliac artery, was oval in shape, and a little flattened. The ureter from the upper kidney (the right) crossed it ventrally and received the ureter from the lower kidney which ran upward to meet it at an acute angle. The openings of the right and left ureters were apparently normal.

The blood supply of the upper kidneys was usual. The lower kidney received an artery from the aorta which entered ventrally, one from the right common iliac dorsally, and one from the hypogastric at the lower pole. The anomaly was found in a sailor who had never experienced any discomfort, and whose death was in no way connected with the kidney abnormality. The renal substance was normal.



FIGS. B AND C.

A similar case is reported by Hyrtl with complete double ureter. In both cases the lower organ was misplaced and pointed hilum ventrally.

B 2. *Fused Supernumerary Kidneys.*

In case the two masses of mesenchyme fuse, three possible results are evident: (a) that the fusion of the two secondary anlages may be so complete and at such an early date that the two parts may act in the same way that one mass does (A 1 and A 2), the abnormality of the ureter being merely visible from the outside; (b) demarkation between the two may be well developed and the kidney form otherwise normal; (c) the fusion may occur at such a late date that one part was rotated before the other became fused to it and this relation would necessarily hold in the adult form.

B 2 a. *Complete Fusion.*

Barlet describes a specimen of supernumerary kidneys in a letter to the Lancet in the following manner: "On examining the kidneys it was found that the subjects possessed three, two on the left side and one on the right. The two on the left side were fused together, one being on top of the other, and externally showed two ureters springing separately along their whole length, opening into the bladder by two distinct orifices, the one being about one-fourth of an inch above the other. On section there was distinct demarkation of the two kidneys which was not visible from the exterior. All three kidneys were normal in appearance and had no connection with the cause of death."

Here is undoubtedly the same condition found in A 2, with both of the sprouts capped by a separate mass of mesenchyme which fused at an early period. It is not mentioned what the relation of the two ureters was, but it is fair to assume that they followed the rule laid down for the complete double ureter. The specimen appeals to me as a strong piece of evidence to disprove the division into an upper and lower pelvis by the growth of the parenchyma.

B 2 c. *Fused Supernumerary Kidneys with One Mass Rotated.*

In the discussion of the cases with double ureter, mention was made that two specimens had been reported by Weigert where the ureter from the upper pelvis did not occupy a ventral position. In the cases cited he found the upper part of the kidney rotated in the usual way, the hilum pointing toward the middle line, while the lower part had the hilum ventrally. He does not mention that these were supernumerary organs, and the following is therefore only inferred from like findings to be taken up later.

The two masses of renal mesenchyme, the secondary anlage for the two parts of the kidney, remained separate until one was rotated at the midlumbar region when the lower and non-rotated part was fused to upper. This would present a result which would correspond with the Weigert cases, and account for the exception to the general rule for double ureter.

Cases of supernumerary kidneys are very rare. Hepburn reports a doubling on both sides in pig, and Amick a similar finding in man. There are still other varieties which will be discussed in a later part of the paper.

C. Changes in Form Involving Both Kidneys.

Thus far only the changes in the form of one kidney have been considered. There are also changes in form which affect both organs, and these are naturally due to a fusion of the two normal masses of renal mesenchyme (Fig. C). It was stated in a very superficial way in the article in "American Medicine" that it might be possible for the two renal buds to lie so closely together that they might be surrounded by one mass of mesenchyme, and that it would be difficult to distinguish this variety from cases of more or less complete fusion. This statement is withdrawn and I do not hold it possible now for two renal buds to stimulate one mass of mesenchyme; there must be two.

The fusion taking place between the masses will, of course, be a permanent one and the condition receives different names, depending on the position and the degree of fusion, but the class as a class is known as the horseshoe kidney. The varieties depend on the manner and degree of fusion.

It was mentioned that the two masses of mesenchyme lie in front of the second sacral vertebra in an embryo of 7.0 mm. (embryo Mall 2) and are at the same level. The renal buds may not lie at the same level and this is due to a slower growth and later date of appearance of one bud as was dealt with in a previous article. I find that one kidney lies a trifle higher than the other in embryo Mall 114, although both organs are still in the true pelvis. Similarly, it is quite possible to conceive that they might lie one above the other or one in front of the other.

C A. Where the masses of mesenchyme are placed at the same level, they may lie:

a. In the same relative position.

b. One ventral to the other.

C B. Where the two masses are placed one above the other:

a. One slightly in advance of the other.

b. The upper pole of one fused to the lower pole of the other.

C A a. Should the two masses of mesenchyme lie in the same relative position and at the same height, three possibilities as to the point of the fusion may be inferred:

1. Fusion at the upper poles.
2. Fusion at the lower poles.
3. Fusion centrally.

C A b. Should the two masses lie one in front of the other, the dorsally placed organ would fuse to the ventral one in such a manner that the hilum of the former would attach to the dorsum of the latter.

C B a. Should one mass of mesenchyme be placed a trifle higher than the other, the relation would be maintained in the fusion, and if one kidney were displaced, it would be the lower one, as would be dealt with more completely in a later paper.

C B b. Should the fusion occur end-to-end, the displacement, as above, will be found in the lower organ.

C A a 1. *Fusion at the Upper Poles.*

In this form of horseshoe kidney the concavity is directed downward, and according to Arneill, is the most uncommon variety. The fusion occurs probably before the organs have grown out of the true pelvis, or as soon as a distinct upper and lower pole have been formed to each mass of mesenchyme (9.0 mm.). The ureter system, being developed from the renal bud, is usually quite normal. The arrangement of the parenchyma joining the kidneys is not known, but there is undoubtedly a more or less definite line of demarkation between the two parts. The earlier the date of the fusion the more indefinite this line would be, and in cases of very late fusion, at about the time that the kidney arrived at its normal height, the growing together might be limited to the capsule. As a rule the capsule is common to both organs.

In a specimen placed at my disposal by Mr. Broedel, there is in addition to other abnormalities a horseshoe kidney fused at the upper poles. The case is unique for this variety of kidney in that the fusion is *behind* the aorta. It will be interesting to work out the arterial defect that allowed the developing masses to slip behind the aorta. The suprarenals, strange to say, were also fused. The blood supply to these organs was naturally abnormal.

Fusion at the upper and at the lower poles not infrequently reaches the normal height, and if the growing together is not too marked, the hila may be rotated to the normal position.

C A a 2. *Fusion at the Lower Poles.*

The most common variety of horseshoe kidney is found in the fusion at the lower poles. It probably has its origin at the same time as the preceding form, and why it should be more common is not known. Many cases have been reported, and as it is only necessary to establish a type in this article, I content myself with referring the reader to the work of Morris on the Surgical Diseases of the Ureter and Kidney, Vol. I, p. 56, where an excellent example of this anomaly is pictured.

The specimen mentioned shows a well-marked bridge of renal tissue connecting the two kidneys at the lower poles. Morris states that the ureters usually lie ventral to the connecting bridge but may lie behind it in case the ureters lie behind the bridge of tissue, the fusion will have been a late one—after the kidneys have been rotated.

The case of Nixon is also alluded to where a similar malposition to that described in the Broedel case was found—fusion at the lower poles and the connecting renal substance behind the aorta. The embryologic defect, probably in the arteria sacra media, which allowed this malposition, would be the same in either case, and will be considered in greater detail in a later paper on the malposition of the kidney.

C A a 3. *Fusion Centrally.*

The central fusion of the two masses of mesenchyme has received the special name of "disc-kidney." The fusion may be so complete that it is difficult to distinguish any line of demarkation between the two kidneys, and the only grosser structure by which the two organs might be identified would be the two ureters opening into the bladder at either side of the middle line.

The case of Haller, pictured in Morris's work, p. 61, is a typical disc-kidney. The organ is situated in the middle line and the two ureters emerge ventrally. A form of fusion which approaches the disc-kidney in its completeness will be mentioned later.

C A b. *Fusion of a Ventrally Placed Kidney to a More Dorsal One.*

The only possibility which remains under A is that in the dorsal growth of the two buds, one came to lie farther back than the other and that fusion took place in this position.

In a case mentioned by Morris, there is a variety of fusion which does not resemble any form of horseshoe kidney thus far described. "The two kidneys formed an irregularly shaped mass which weighed thirteen ounces, and was lying on the front of the promontory of the sacrum. It was not horseshoe-shaped and the vessels and ureters were arranged most unusually. The central part of the mass was fissured by a sulcus, in which the ureter for the left kidney coursed downwards and the vein for the same upwards, passing into the vena cava just above the junction of the two iliacs. In the right half of the mass the ureter and vessels, instead of being situated centrally, were on its outer side; the ureter being in front of the vessels as on the left and as is usual in fused kidneys." "The renal substance, to the naked eye, was healthy."

I think this explanation of the anomaly could be made: That the two masses of mesenchyme were normally placed

excepting that one was in front of the other, and that a fusion occurred between the front edge of the dorsal mass (about the hilum) and the touching edge of the ventrally situated mesenchyme. Both organs were in the pelvic inlet and a later rotation, probably a purely mechanical one to gain room, turned both ureters toward the same side. The one would in this case undergo a normal rotation and the other, one in the opposite direction. In the specimen of two kidneys pictured by Morris, one must have been placed a little in front of the other.

C B a. *Fusion of a Lower Kidney to a Higher One.*

In all the variations in the form of the two kidneys thus far considered the two organs were placed at the same level. In embryo Mall 114 (10.0 mm.) one kidney was found lying a trifle higher than the other, although both organs were still in the true pelvis. Should a fusion occur the lower kidney would remain in the lower position.

This type of fusion is found in a case of horseshoe kidney placed at my disposal by Dr. W. H. Lewis. The two kidneys lie on the midline and the right organ is a trifle higher than the left. The mass is somewhat irregular, but the two kidneys are well divided by a longitudinal fissure. The ureters emerge ventrally and empty normally in the bladder. The mass was in a low position and lay upon the bifurcation of the aorta.

These minor differences in height are difficult to tell from disc-kidney, but as a rule the two parts are more distinct. When the difference in the height is more marked, and the organs lie above the point of rotation, the lower kidney is usually displaced and crosses to the opposite side—crossed dystopia (see McMurrich's article).

The fusion of a higher kidney to a lower kidney may be any variety from a disc-kidney to an end-to-end fusion which is discussed in the next sub-heading. The blood supply to these organs is more or less abnormal, depending on the degree of the malposition. Normally placed horseshoe kidneys may have a normal blood supply.

C B b. *End-to-end Fusion.*

In a case reported by Broesicke, two kidneys were fused end-to-end and both organs were placed to the left of the middle line. The arrangement of the ureters was strikingly abnormal. The upper ureter arose from the mesial surface of the mass and the lower one from the lateral side. The openings of the ureters in the bladder were normal. The specimen is one of "sigmoid kidney." Broesicke agrees with Schultze that the anomaly is explained on the basis of the embryology.

Here the two masses of mesenchyme were placed one above the other and fused after the rotation of the upper kidney took place. The case is similar to the variety discussed under B where the upper half of the kidney rotated and then became fused to the lower part.

These end-to-end fusions are all of relatively late stages. Should the two masses fuse at a very early date, there would be difficulty in distinguishing the two kidneys. The mass would be different from the centrally fused horseshoe kidney in that the ureters would be placed one above the other. This form of kidney is reported by Morris and pictured on page 49. The variety is interesting in the discussion of the causes of the rotation.

C C. *Fusion of Supernumerary Kidneys of Opposite Sides.*

Granting that the doubling of the kidney may be found on one or both sides and that fusion between the masses of mesenchyme on the same and opposite sides may take place, a number of combinations may occur which are represented in the scheme below. Naturally all these cases have not been reported, but this does not preclude the possibility of their being found. It must be remembered that fusion between a normal mass of mesenchyme on one side and two masses on the other may also occur, and the resulting form is easily deduced from the scheme.

In the first series, the upper and lower masses are presented as remaining free:

a. Horseshoe kidney with free supernumerary kidneys below.
b. Horseshoe kidney with free supernumerary kidneys above.
c. Double horseshoe kidney (no cases reported).

In the second series, the upper masses are fused to the lower:

d. Horseshoe kidney with fused supernumerary kidneys below.
e. Horseshoe kidney with fused supernumerary kidneys above.
f. Fusion of all four parts (e and f reported).

In the third series, the organs are placed at different levels:

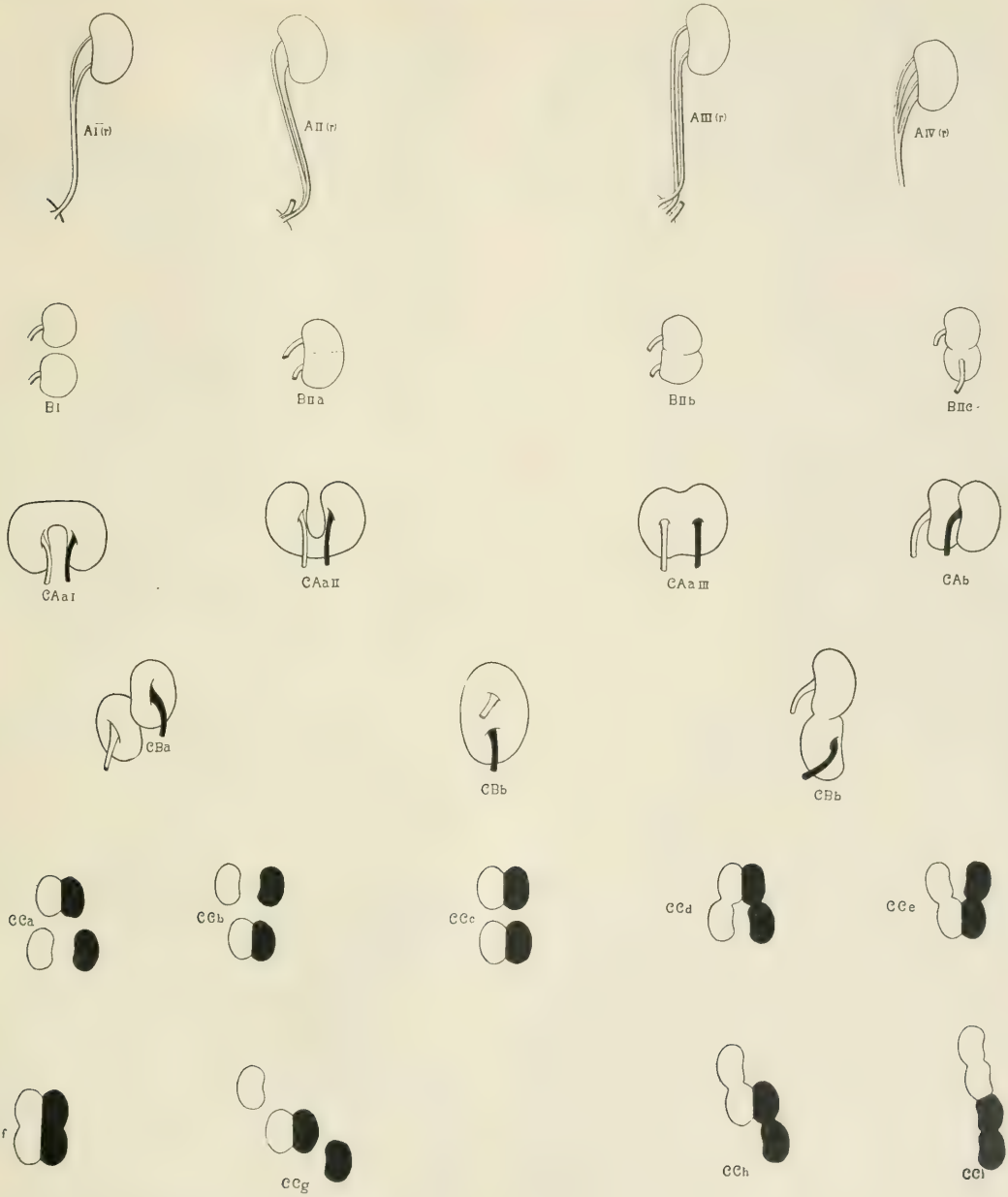
g. Horseshoe kidney with free supernumerary above and below.
h. Horseshoe kidney with fused supernumerary above and below.
i. End-to-end fusion of all four parts (none reported).

C C e. *Horseshoe Kidney with Fused Supernumerary Kidneys Above.*

A specimen is described by Oleson of four kidneys in a human being. The mass was fused at the lower poles, and on each side there appeared to be a division into two. From the report it is gathered that the ureters were incompletely doubled, and that the author identified the two supernumerary organs above.

C C f. *Fusion of All Four Parts.*

Morris pictures an anomalous kidney mass, p. 54, the case of Batallus, which I take to be the fusion of four kidneys. The mass presents "a quadrilateral appearance" and each ureter divides into two. There is, of course, a question as to the definiteness of this statement, but the case seems to conform, and there is no reason why double kidneys on either side should not behave like a central fusion of the disc-kidney variety.



There are some abnormalities which are not included in this paper, and only those have been mentioned which seem to find an explanation in the development of the tract. The embryology of these anomalies is not very complicated when one follows the development closely. The supernumerary kidney, like the double ureter, has a distinct importance in the study of normal embryology, and serves to substantiate the rule which was assumed in the first part of this article,

that abnormalities in form are dependent on small variations in the development of the renal bud and mesenchyme before the embryo reaches a size of 10.0 mm.

The letters and numbers of the figures in the plate correspond to the numbers and letters in the paper, and to simplify matters, all those which have been reported are marked with an (r). In the schemas of the horseshoe kidneys, the one ureter has been pictured black, and in the supernumerary kidneys the ureters have been omitted and the one side made black; the concave side representing the hilum in each.

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ON THE FIRST APPEARANCE OF THE RENAL ARTERY, AND THE RELATIVE DEVELOPMENT OF THE KIDNEYS AND WOLFFIAN BODIES IN PIG EMBRYOS.

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A review of the literature on the development of the kidneys and Wolffian bodies in pig embryos, shows but little concerning the blood supply and the relative size of these organs. Perhaps the most extensive study is found in Keibel's Normentafel, in which the anlages and subsequent development of these glands are traced histologically. Here, however, no measurements except those of the embryos are given. In the accounts of the embryology of the arterial system there is no work which shows the relative development of the blood supply to these two glands. At the suggestion of Dr. Pohlman, I measured these organs in pig embryos, and made a number of arterial injections. These injections demonstrate the first appearance and development of the renal artery and afford an opportunity to compare the blood supply of the kidney and Wolffian body in pig embryos ranging from 20 mm. to 75 mm. in length. The measurements show the relative size of these glands at various stages from 20 mm. to 132 mm.

Material and Methods.—The abundance of material from the slaughter houses offered every facility for numerous measurements and repeated injections upon live pig embryos, while the valuable collection of human embryos belonging to Professor Mall afforded opportunity to compare the human fetal development with that of the pig. The pig embryo is especially adapted for the study of the Wolffian bodies because of the relatively larger development of this organ in the pig than in man or rabbit.

Measurements.—As each uterus was opened the vertex-breech lengths of the embryos were made and measurements of the kidneys and Wolffian bodies were taken. These measurements were then averaged and the results were used in plotting the curves of their relative development. In cases where the growth of these organs was abnormal, their measurements were not included in the averages.

Injections.—In making injections, India ink, diluted to one-third of its commercial strength, was used.[1] In certain instances, pure water formed a precipitate, when added to the

[1] Taguchi's method modified. Arch. f. Mikr. Anat., 1888.

commercial ink, but this could be easily remedied by the addition of a small amount of weak ammonia. Lamp-black solutions proved to be most unsatisfactory, because of the difficulty in obtaining solutions of similar consistency. Frequently, also, this injection mass would clog the needle of the syringe. All injections were made through the hypogastric artery before the embryo was removed from its surrounding membranes. In this way the organism was protected from undue pressure and from injury in handling. During the operation, the embryo still attached to a portion of the uterine wall was immersed in warm water. A ligature was passed around the umbilical cord close to the wall of the uterus, thereby preventing infusion of the injection mass through the uterine tissues. The hypogastric vein was then pricked with a needle, thus reducing the pressure in the circulatory system consequent upon the entrance of the injection fluid. All injections were made with a fine hypodermic syringe by piercing the hypogastric artery close to the abdominal wall. To obtain an even flow it was necessary to have a perfectly adjusted syringe devoid of all capacity markings. With such a syringe an even pressure of about one drop in three seconds was maintained with little difficulty. By watching the femoral arteries the progress of the fluid was followed and an injection without extravasation was obtained. After the injection, the membranes were removed and a measurement of the body length was taken. Then an abdominal incision was made and the liver and portions of the intestines were dissected away, exposing the kidneys and Wolffian bodies. In the smaller stages it was necessary to displace the Wolffian body in order to obtain a measurement of the kidney, as at this time it is completely hidden by the larger gland. The positions of these organs relative to the vertebral column were also noted, though this was more easily discerned after clearing.

Clearing.—To clear the specimens, the Schultz method, modified by Dr. Mall, was used. The specimen was first thrown into 95 per cent alcohol until completely shriveled. As a rule forty-eight hours were sufficient to accomplish this result. Then the upper portion of the embryo, just above the twelfth thoracic vertebra, was dissected off, leaving the Wolffian bodies and the kidneys attached to the body wall. Thus during the clearing in a 2 per cent solution of sodium hydroxide, which followed, the action of the reagent could be watched and controlled. This usually took from four to eight hours. When the tissues had become translucent in this medium the specimen was transferred to 20 per cent glycerine for a week or more, and was then placed in absolute glycerine where it became transparent. Upon complete clearing the vertebral column was shown quite prominently and its position relative to the kidneys and Wolffian bodies was noted. In this absolute glycerine the organs became so firm that the remaining portions of the body wall were removed and the specimen was then placed between watch crystals for microscopic study.

Injections were also attempted through the liver while the embryo was alive, but the vascularization of the Wolffian bodies is such that venous injections were most unsatisfactory. The causes of this will be taken up later.

TABLE SHOWING THE LENGTH IN MILLIMETERS OF THE KIDNEYS AND WOLFFIAN BODIES OF PIG EMBRYOS.

The measurements were made from vertex to breech, and include all of the embryos in each uterus. In case of asymmetric development of these glands in any embryo averages were made of the lengths of both organs.

RELATIVE SIZE OF THE KIDNEY AND WOLFFIAN BODY AT DIFFERENT STAGES.

	Vertex-Breech.	Kidney.	Wolffian Body.
Uterus 1	20	1.2	7.3
	21	1.2	7.3
	20	1.1	7.4
	23	1.2	7.2
	22	1.3	7.1
	21	1.0	7.3
	20	1.2	7.2
Uterus 2	28	2.5	9.0
	28	2.6	8.0
	29	2.5	8.5
	27	2.4	9.2
	28	3.0	7.0
	29	2.7	8.7
Uterus 3	30	2.8	8.6
	32	3.2	8.8
	30	3.5	8.7
	33	3.4	8.8
	29	2.9	8.9
	34	3.5	8.7
Uterus 4	31	3.9	9.2
	33	4.0	9.1
	33	3.8	9.0
	35	3.7	9.1
	33	4.1	8.9
Uterus 5	38	5.0	10.0
	39	5.5	9.5
	38	5.5	10.0
	38	5.0	10.0
	39	5.0	10.0
	39	6.5 abnormally large.	8.5 abnormally small.
Uterus 6	39	5.5	10.0
	39	5.5	9.5
	38	5.7	9.5
	39	5.5	10.0
	40	5.6	10.2
Uterus 7	40	5.8	10.0
	41	5.9	10.0
	40	5.9	11.0
	42	5.9	11.0
	41	5.8	10.0
	43	6.0	11.2
	41	5.8	10.5
	42	5.9	11.3
	39	5.6	11.5
	41	5.9	10.0
Uterus 8	49	8.0	11.5
	48	7.0	12.0
	48	6.5	11.1
	49	6.0	12.0
	48	7.0	10.0
	49	7.3	11.0
	48	7.5	11.5
	49	8.0	10.5
Uterus 9	49	7.3	11.0
	49	7.8	10.5
	49	6.8	12.0
	48	8.0	10.0
	50	7.8	10.5
Uterus 10	57	9.2	11.5
	57	9.0	11.4
	56	9.2	11.2
	58	9.0	11.5
	57	9.3	11.0
	59	9.5	11.5
	58	9.0	11.4

	Vertex-Breech.	Kidney.	Wolffian Body.
Uterus 11	60	9.2	11.5
	59	10.6 abnormally large.	9.8 abnormally small.
	57	9.5	11.4
	61	9.4	11.5
Uterus 12	62	9.4	11.5
	60	9.3	11.0
	64	9.5	11.7
	60	9.0	11.3
	64	9.5	11.0
	63	9.7	10.5
Uterus 13	67	11.5	11.5
	67	11.5	11.0
	69	11.0	12.0
	70	11.5	11.0
	67	11.4	11.5
	67	11.5	11.0
Uterus 14	68	11.7	11.8
	67	11.5	12.0
	68	11.5	11.4
	69	11.4	11.5
	67	11.2	11.2
	68	11.5	11.7
	67	11.6	11.4
Uterus 15	84.5	14.4	10.0
	84.5	14.5	10.0
	84.0	15.0	10.0
	85.0	14.6	9.5
	84.5	14.2	11.0
	84.0	14.0	11.0
	85.0	17.2 abnormally large.	8.0 abnormally small.
Uterus 16	85.0	14.5	10.2
	84.6	14.7	10.0
	84.4	14.3	10.5
Uterus 17	90.0	15.0	9.7
	91.0	15.3	9.5
	90.0	15.0	9.7
	89.5	14.6	10.0
	90.1	15.0	9.6
Uterus 18	94.3	15.7	9.2
	94.5	15.9	9.0
	94.3	15.6	9.0
	94.0	15.5	9.8
	94.4	15.7	8.7
	94.3	15.6	8.9
Uterus 19	112.2	18.3	7.1
	112.5	18.4	7.0
	111.9	18.0	7.1
	112.0	18.0	6.7
Uterus 20	120.6	19.4	5.6
	121.0	19.6	5.4
	120.8	19.5	5.5
	120.7	19.5	5.5
Uterus 21	132.4	20.0	At this stage the Wolffian
	132.6	20.3	bodies have become so atro-
	131.9	21.0	phied at the anterior end
	133.0	20.5	that accurate measurements
	132.5	21.0	are impossible.
Uterus 22	155.1	23.6	
	156.9	23.8	
	157.2	24.0	
	155.5	23.8	

A study of the foregoing tables shows comparatively little variation in the body lengths of the embryos in each uterus. In the cases of abnormal development of the kidney, it is interesting to note the corresponding size of the Wolffian body. That a balancing of function exists between these two glands is suggested by the fact that an embryo having an unusually large kidney development has correspondingly small Wolffian bodies.

In the accompanying diagram, the curves are constructed from the foregoing measurements and represent the growth of the kidney and Wolffian body as compared with the general development of the embryos. In the case of the Wolffian body it is impossible to properly depict the atrophy of this gland by a curve, because the degeneration which occurs mainly in the cephalic end is marked rather by a decrease in width than in length.

Embryological Development of the Wolffian Body and Kidney.—As is well known, the Wolffian body finds its anlage in the Wolffian duct which is developed as a solid mesoblastic cord of cells, lying close to the vertebral column in the abdominal cavity. This cord of cells acquires a lumen and penetrates the urogenital portion of the cloaca. Adjacent to the anterior end of this duct on the outer side lie the mesoblastic cells which later become the Wolffian body. The rapid growth of this gland from the 7 mm. stage to that of 10 mm. has been described by Allen.[2] He states that between 7 mm. and 8 mm. the Wolffian body is almost doubled in size, while at 10 mm. it is half as broad again, and has also increased dorso-ventrally. MacCallum has found at this same stage of 8 mm. well-formed glomeruli and tubules throughout the whole length of the organ.[3] The Wolffian duct is also fully developed and according to Minot is larger proportionately at this stage than at any time later.

The Wolffian bodies are elongated structures attached to the mesentery close to the dorsal wall. The anterior and posterior ends curve toward the median line, though the curve is more exaggerated in the case of the former. The anterior end tapers slightly when the gland is at its fullest development, and it is in this portion that atrophy begins. The Wolffian duct lies as a ridge on the flat dorso-lateral surface of the gland and extending from the anterior end empties into the urogenital part of the cloaca. During its course across the organ it sends out at regular intervals tubules which are very much contorted and almost encircle the periphery of the organ. The arteries supplying the gland penetrate the dorso-medial portion and form with the distal end of these tubules glomeruli similar in structure to those of the true kidney, though slightly larger.[4]

The venous system in this gland consists of branching capillaries which follow the periphery and anastomose profusely in the midst of the organ. Injections consequently resulted in almost solid masses of black with no definite structure. The relation of the arteries and veins is easily discerned by sections and shows a vascular arrangement similar to that of the kidney. The arteries and veins in the glomeruli are sur-

[2] Allen, B. M., Embryonic Development of Ovary and Testis of Mammals, American Journal of Anatomy, Vol. III, No. 2.

[3] MacCallum, J. B., Notes on the Wolffian bodies of Higher Mammals, American Journal of Anatomy, Vol. I, No. 3.

[4] MacCallum, op. cit.

rounded by an epithelial membrane similar in structure to Bowman's capsule of the kidney, and the histological structure of the tubules is also quite similar. Each tubule begins at the glomerulus as a somewhat constricted tube and widens in the middle, narrowing again before reaching the duct. The space between the tubules, according to Minot, is lined with epithelium and gives evidence of a sinusoidal circulation.

Kidney.—The kidney, as has been long known, arises as a tubular diverticulum from the Wolffian duct near its entrance into the cloaca. This broadens at its distal end, forming the renal pelvis, while the tubular portion becomes the ureter. When the embryo is 12 mm. in length the pelvis of the renal anlage is between the fifth lumbar and second sacral vertebrae, just below the division of the dorsal aorta into the right and left hypogastric arteries.[5]

From this stage in the development of the kidney and Wolffian body, which has already been so thoroughly worked out, the following figures trace the relative development of these glands and their blood supply.

It was found best in order to avoid confusion to omit from the drawing the adrenal glands, ureters and Wolffian ducts as well as the ovary or testis. In this way the comparison between the Wolffian body and kidneys is more easily illustrated.

In Figure 1 the kidney is moving in a cephalic direction toward its permanent position and has at this stage received no apparent blood supply. To ascertain that no injection had reached the organ it was completely mascerated and studied under high power. No suggestion of arterial supply was discovered and it is probable that the renal arteries in the pig embryo as in the human fetus do not penetrate the kidneys until they have reached their permanent position. It was supposed that these arteries might enter the kidneys earlier and grow up the aorta as the organ ascended, but injections and examinations of sections show no vascularization until the kidney has reached its permanent position. That the absence of injection fluid in the kidney at this stage was not due to imperfect injection is evinced by the fact that the finest capillaries of the lower extremities and viscera are completely filled.

As in the human embryo, rotation of the kidney occurs before the entrance of the blood supply. According to Pohlman, this rotation takes place in the human embryo at 14 mm.[6] My study of sections of pig embryos places the rotation of the

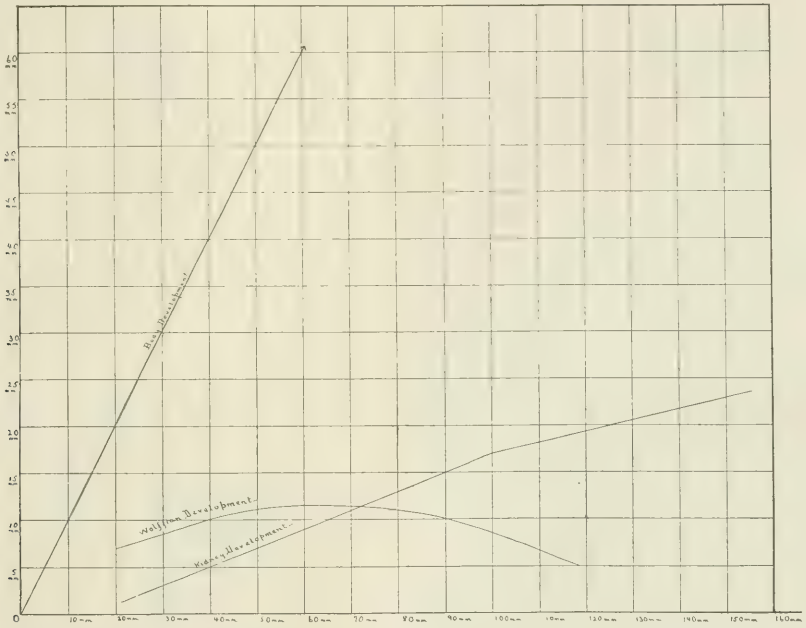


Diagram showing the relative size of the kidney and Wolffian body as compared with the length of the embryo.
Averages were made of the measurements of the embryos in each ulterus except in certain cases of abnormal development, when only the average of those normally developed was taken.

[5] Lewis, F. T., The Gross Anatomy of a 12 mm. pig, Vol. VII, Americal Journal of Anatomy.

[6] Pohlman, A. G., Concerning the embryology of Kidney Anomalies, American Medicine, Vol. VII, No. 25, pages 987-990.

kidneys in this genus between 12 and 15 mm. The vascularization of these glands in the human fetus, as has also been proved by Pohlman, takes place during the time the embryo is increasing in length from 25 mm. to 30 mm. In the pig embryo, the first appearance of the renal artery which I have been able to demonstrate, occurs at 28 mm.

The Wolffian bodies at this stage are highly vascularized and the glomeruli are fully developed.

The number of arteries leading from the aorta to these glands during the early stages is approximately the same, while the increase in size is proportional to the body growth.

Figure 2 shows the entrance of the renal artery at the earliest stage, though only a very slight arterial supply to the glomeruli was discernible. The Wolffian body is more highly vascularized and has broadened and lengthened.

In Figure 3 the glomeruli of the kidney have received their arterial supply while the Wolffian arteries have increased considerably in diameter. The organ has also increased in size. The heavy injection shown in the dorso-medial region indicates as in the first two figures the region of the glomeruli. It is around these that the tubules end. The position of the organs relative to the vertebræ is but slightly changed. At this stage the development of these vertebræ and the kidneys and Wolffian bodies seems quite proportional.

Figure 4 shows the rapid increase in the vascularization of the kidney and its relative growth. A slight atrophying of the anterior portion of the Wolffian body has begun, and the arterial supply of the glomeruli of this part of the gland is less extensive than in the posterior end, where the blood supply still continues to increase.

In Figure 5 the four anteriorly situated arteries to the Wolffian body have decreased in diameter and the accompanying glomeruli show consequent lack of blood supply. The posterior glomeruli on the other hand are still well vascularized, and there is no atrophy of the gland itself in this portion. The kidney manifests a further development, both in the number of its glomeruli and in its uniform growth.

In Figure 6 it was found to be impossible to separate the two glands so that we find the Wolffian body closely attached to the lower ventral border of the kidney. The atrophy of the anterior portion of the Wolffian body has become most evident, though this degeneration is more manifest in width than in length. The glomeruli in this part of the gland have practically no blood supply and several of the arteries have entirely disappeared. By this time the cortex of the kidney has become so thickened that only the blurred outlines of the arteries are discernible.[7]

Figure 7 shows the complete disappearance of the anterior Wolffian arteries and the absence of glomeruli in this portion of the gland. Three of the posterior arteries still persist and supply the glomeruli of this part of the organ, though one of these seems ready to atrophy. In the kidney development there is little more to be noticed except a general increase in size and blood supply.

Injection methods give no further information concerning the Wolffian body after this stage. It is well known, however, that the anterior portion continues to rapidly diminish in width and later in length, and that the remaining tubules are finally claimed by the testis or ovary.

In the male the Wolffian duct becomes the canal of the epididymis, the vas deferens and the common ejaculatory duct, and the remains of the gland itself become the vasa afferentia, ductuli aberrantes and the rudimentary paradidymis.

In the female, the duct becomes the longitudinal duct of the parovarium and the hydatids of Morgagni, while the tubules of the Wolffian body are transformed into the rudimentary tubules of the parovarium and of the paroophoron.

SUMMARY.

A. The renal artery penetrates the kidney when the embryo has attained a length of 28 mm.; rotation of this gland having occurred between 12 mm. and 15 mm.

B. A balancing of function is suggested by a study of the measurements of these glands.

C. As the blood supply to the kidney increases there is a corresponding atrophying of the Wolffian arteries.

D. Atrophy of the Wolffian arteries is first evident when the embryo is 45 mm. in length.

E. As atrophy of the Wolffian body itself continues, the sex gland becomes more firmly attached to the posterior portion, and the remaining tubules and duct are claimed by the ovary or testis.

Before completing this article, I wish to thank Professor Keibel, of the University of Freiburg, for the privileges of his laboratory, in which a portion of this work was done.

[7] Recent injections which were cleared in a saturated solution of sodium hydroxide instead of a 2% solution bring out quite distinctly the course and distribution of the renal arteries and the location of the glomeruli in the kidneys of pig embryos 68 mm. and 75 mm. in length. The general arrangement of these arteries and glomeruli is similar to that found in figure five.

INSTRUCTION IN PSYCHIATRY AND NEUROPATHOLOGY.

A limited number of graduates in medicine can have an opportunity for work in the laboratory of the Sheppard and Enoch Pratt Hospital.

Instruction in neuro-pathology will be given by the director of the laboratory, and those attending the course will be permitted to attend the clinical and other conferences of the medical staff. Clinical forms of insanity will be discussed, as well as the hospital and home care of the insane.

Physicians taking this course will also have an opportunity to attend the neurological clinics at the Johns Hopkins Hospital.

For particulars, apply by letter to Dr. E. N. Brush, Physician-in-Chief and Superintendent, Sheppard and Enoch Pratt Hospital, Station "A," Baltimore.

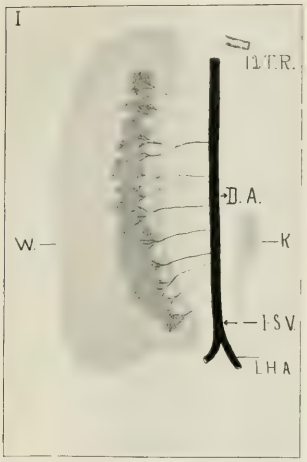


FIG. 1.—The right Wolffian body and the left kidney of a pig embryo 20 millimeters long; injected through the hypogastric artery with India ink. The length of the Wolffian body is 7.3 mm., and the kidney is 1.2 mm. long. D. A., dorsal aorta. K., kidney. L. H. A., left hypogastric artery. W., Wolffian body. 12 T. R., twelfth thoracic rib. 1 S. V., first sacral vertebra.

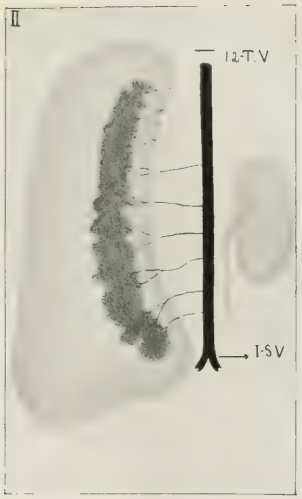


FIG. 2.—The right Wolffian body and the left kidney of a pig embryo 28 mm. long; injected through the hypogastric artery with India ink. The entrance of the renal artery is first demonstrated at this stage. The length of the Wolffian body is 8.5 mm., and the length of the kidney is 2.6 mm. 12 T. V., twelfth thoracic vertebra. 1 S. V., first sacral vertebra.

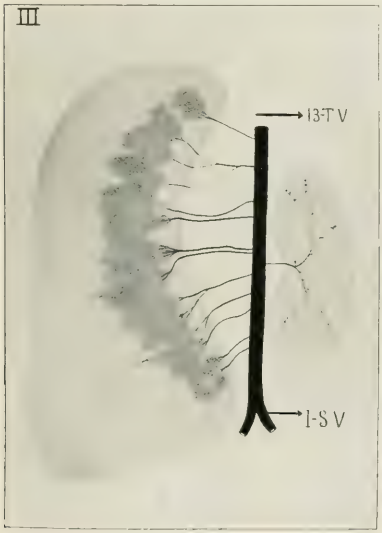


FIG. 3.—The right Wolffian body and the left kidney of a pig embryo 33 mm. long; injected through the hypogastric artery with India ink. The length of the Wolffian body is 9.1 mm., and the kidney is 3.9 mm. long. 13 T. V., thirteenth thoracic vertebra. 1 S. V., first sacral vertebra.

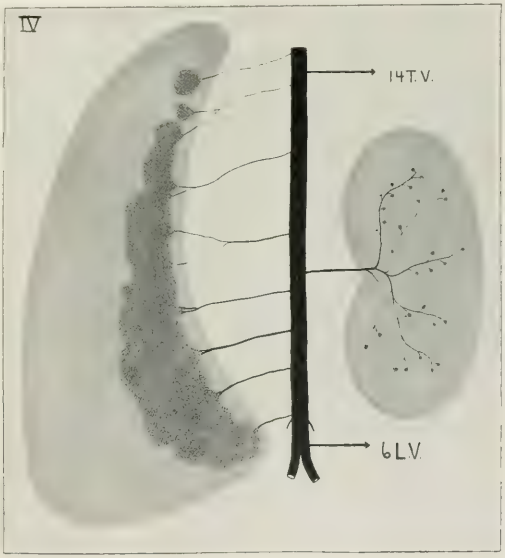


FIG. 4.—The right Wolffian body and the left kidney of a pig embryo 45 mm. long; injected through the hypogastric artery. The length of the Wolffian body is 10.6, and the length of the kidney is 6.3 mm. 14 T. V., fourteenth thoracic vertebra. 6 L. V., sixth lumbar vertebra.

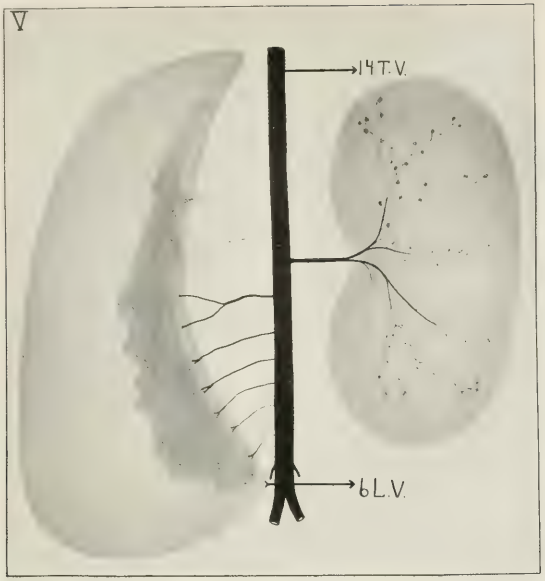


FIG. 5.—The right Wolffian body and the left kidney of a pig embryo 54 mm. in length; injected through the hypogastric artery. The length of the Wolffian body is 11.2 mm., and the length of the kidney is 8 mm. 14 T. V., fourteenth thoracic vertebra. 6 L. V., sixth lumbar vertebra.

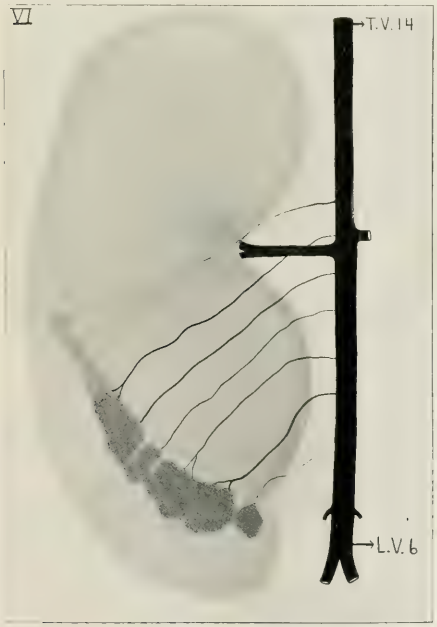


FIG. 6.—The right Wolffian body and right kidney of a pig embryo 68 mm. long; injected through the hypogastric artery with India ink. The length of the Wolffian body is 11.3 mm., and the length of the kidney is 11.5 mm. 14 T. V., fourteenth thoracic vertebra. 6 L. V., sixth lumbar vertebra.



FIG. 7.—The right Wolffian body and right kidney of a pig embryo 75 mm. long; injected through the hypogastric artery with India ink. The length of the Wolffian body is 10.9 mm., and the length of the kidney is 12.2 mm.

HIGH BIFURCATION OF THE BRACHIAL ARTERY WITH REUNION AT THE ELBOW.

By Minerva Herrinton.

The abnormality herewith reported is of interest because it blends three variations, which, taken alone, are not common in one specimen. The specimen is from the left arm of a white woman, 50 years old, whose death was caused by acute aneurysm (No. 1131). It was my good fortune to dissect this arm while a student of anatomy at the Johns Hopkins University, and with the permission of Dr. Mall I report it.

The axillary and brachial arteries are normal in arrangement until the middle third of the arm is reached. Then between the middle and lower thirds of the arm the artery divides into the ulnar and radial arteries, which are about equal in size. These branches continued somewhat separated until they passed the elbow, when they came in apposition and anastomosed by an opening about as large as the lumen of either of the arteries. The accompanying figure, which is drawn at one-fourth scale, shows the dimensions, form and relation of the arteries. The anastomoses with the posterior ulnar recurrent and anastomotica magna are also shown.

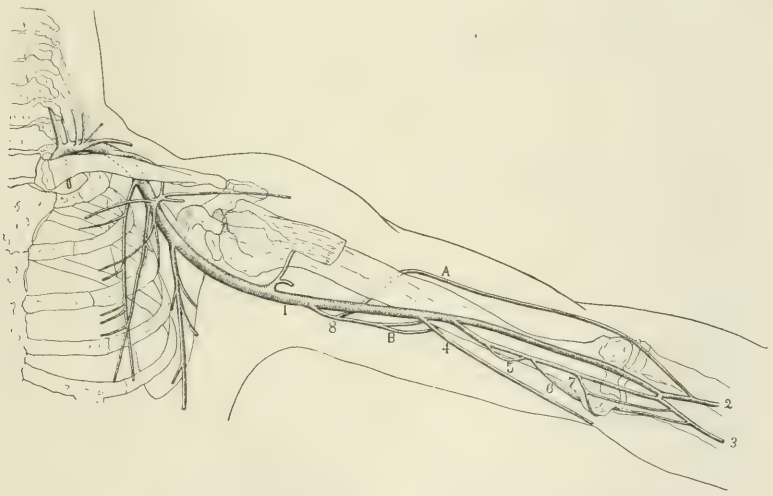


Fig. 1.—Outline of the Brachial Artery and its Branches. Reduced. 1, brachial artery; 2, radial; 3, ulnar; 4, branch accompanying ulnar vein; 5 and 6, branches anastomosing with the posterior ulnar recurrent and anastomotica magna; 7, anastomotica; 8, superior profunda; A, branch accompanying the musculospiral nerve; B, branches to muscles and the anastomoses around the elbow joint.

A specimen in the Army Medical Museum at Washington, prepared by Dr. D. S. Lamb, shows a similar variation, high division of the brachial artery with partial reunion at the usual site of its bifurcation into the radial and ulnar. Similar cases are also reported by Quain,[1] Henle,[2] Tiedemann,[3] Power,[4] Green,[5] Maestre [6] and others, which together indicate that there must be some force which favors the bifurcation of the brachial artery at the elbow and that if it bifurcates higher this same force has a tendency to reunite the branches as shown in these cases.

Without entering into the discussion of the arteries of the early embryo, it may be noted that in their later development those arteries which are more favored are preserved. Such branches pass to the ulnar and radial muscle masses and then are arranged on either side of the humerus and later slide down to the forearm. In case the brachial artery bifurcates while the muscle masses are high and obstacles are then placed between the two branches, the condition continues during life. If the bifurcation is low, say the lower third of the humerus, there is no marked obstacle, and by a process of union and shifting the two arteries may unite until they reach an obstacle, which is at the usual point of division. For this reason a bifurcation in the lower third of the upper arm is rare. In this case some obstacle prevented such a union all the way down, but since these arteries were again close together at the usual point of bifurcation, one of the many small branches which united them at this point in the embryo enlarged, for it was "put into use frequently," so to speak. From this time on there was a balance which favored the circulation first through one of the channels of the bifurcation and then through the other, which of necessity caused blood to flow through the anastomosis. Had this not been so, one of the

two channels would have been obliterated or the anastomosis would have closed, as under similar conditions the foramen ovale, ductus arteriosus and other vessels become obliterated.

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A preparation by D. S. Lamb, Act. Asst. Surg. U. S. A., in the Army Medical Museum is that of a dissected and injected right arm showing high division of the brachial artery with partial reunion at the usual site of bifurcation into the radial and ulnar.

FIXATION OF TISSUES BY INJECTION INTO THE ARTERIES.

By Burton D. Myers, M. D.,

Associate Professor of Anatomy, University of Indiana.

During the past year, while preparing tissues for the course in histology at Johns Hopkins University, the injection method recommended by McFarland [1] of Leland Stanford, Jr., University, was given a trial. The result was so excellent as to lead to its continued use.

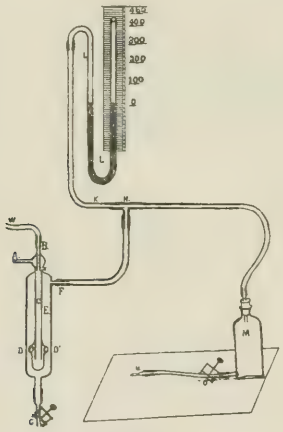


Fig. 1.

The method as suggested by McFarland is very simple. Two bottles with an outlet near the bottom are fitted up with tubes and clamps. This system is to be run up by means of rope and pulley to such a height as will give the gravity pressure required. Simple as the method is, it is very effective. It has, however, the disadvantage of being somewhat inconvenient to handle, and of giving no satisfactory registration of the pressure used, for the pressure varies not alone with the height of the injection flask, but with the specific gravity of the injection mass. Moreover, the method is such an excellent one that some of the more expensive fixing agents were experimented with, which would have been out of the question if one had to fill up an extensive injection apparatus, consisting of a flask and six or seven feet of rubber tubing, with so expensive a fixer as Hermann's fluid, for instance. Still further, it is entirely too difficult to keep so extensive a system as warm as is necessary for a fine injection of blood-vessels with carmine gelatin. Therefore connection was made, in the laboratory, with a very effective air-blast run by water pressure, and this in turn gave place to the inexpensive apparatus figured below. As will be seen readily, the figure illustrates a blast apparatus. The tube *W*, leading from a water tap, is attached to a glass tube *B*, a part of the apparatus. This glass tube *B* ends at *x*, a constricted portion of a chamber to which the air has free access through the tube *A*. Water passing through the system leaves the tube *B* at *x*, drawing along with it a quantity of air into the tube *C*. The force of the water in this tube *C* is broken by the cap at its lower end, and the water and air escape through the openings *D* and *D'* into the chamber *E*, out of which there are but two ways of escape, one at *F* and the other at *G*. The escape of the water at *G* is regulated by a screw clamp according to the air pressure desired. In the chamber *E*, the air, of course, rises to escape at *F* through the rubber tubing connecting *F* with the *T* tube interposed at *H*, through one arm of which connection is established, *J*, with the injection flask *M*, and through the arm *K* connection is made with the mercury manometer *L*.

It is obvious that in the chamber *E* and in the tubes *F J K* and in the flask *M* the air pressure is the same, and will be registered on the millimeter scale placed back of the open leg of the manometer.

On this scale the reading is doubled, for the mercury falls

[1] Jour. of App. Microscopy, Vol. II, No. 10.

in the closed as much as it rises in the open arm, and the difference between the columns is the sum of the rise plus the fall, or double the rise.

Let us suppose our animal, preferably a young one, killed, the artery exposed, and the ligatures in place ready for tying in the glass canula *N*. Let us suppose the injection flask filled with 300 or 400 cc. of normal salt solution heated to 38 or 40° *C.*, and the cork in place, through which, by means of a glass tube, connection between *J* and *M* is established. Now loosen the screw clamp at *O* just enough to let the 12-inch tube and the canula *N* fill with the injection mass and drive out all the air. Now cut the artery, insert the canula and tie it in place. Then cut one of the large veins, say the inferior vena cava, to permit the washing out of the vessels, turn on the water at the tap and loosen the clamp at *O*. If only a little water is turned on, the water and most of the air escape at *G* and the air pressure remains very low. Even if the full water pressure is turned on, if the escape at *G* is too free, considerable air escapes that way and the air pressure remains low. Therefore, when a good flow of water is established, gradually tighten the screw clamp at *G*, at the same time watching the manometer; the water begins to back up in the chamber *E*, escape for the air at *G* is cut off, and the air pressure rises. Thus a balance may be established between the water pressure used and the air pressure.

If the water in the chamber *E* rises much beyond the openings *D D'*, the clamp at *G* must be loosened a bit, or the water will back up into the tubes *F K J* and then over into the flask *M*.

The limit of the pressure to be secured with this apparatus depends upon the water pressure, which, however, is usually much greater than should be used for injection. It is usually possible to get a pressure of 240 to 250 mm. mercury, i. e., a 5-pound pressure, and as a rule one-fourth of this is sufficient.

When the vascular system is well washed out by the normal salt solution, clamp off the flow at *O*, turn off the water at the tap, pour out the remaining normal salt solution, fill the flask as full as desired with the fixing agent heated to 40° *C.*, and again begin the injection.

With this method any rapid fixer may be made use of. It is not always necessary to wash out the blood-vessels with normal salt solution. Fixation is usually better, however, for having done so. With mercuric bichloride it does not so much matter. With formalin and Hermann's fluid, however, it is advantageous for fine fixation. The best fixers have proven to be mercuric bichloride, formalin, Hermann's fluid, and alcohol.

By this method the tissues, after a few minutes bath in warm normal salt solution, are instantly penetrated to the last cell by the fixing agent. The advantages are very great. The tissues, within a few minutes after anæsthetizing the animal (for anæsthetizing, illuminating gas is recommended as being cheap, and causing no salivation), are perfectly fixed in a normal position, at normal distention, and during normal activity. The possibility of post-mortem changes in the central nervous system is practically eliminated. The processes of digestion and absorption are arrested and fixed in the act, and tissues may thus be secured in any desired stage of physiological activity. Engorged tissues are caught with the blood in them, giving a picture of rare beauty. Blood and bone marrow are perfectly fixed.

For studying bone marrow the ribs of a kitten or baby rabbit fixed with $HgCl_2$ will decalcify over night in a solution of 3 per cent HNO_3 made up with 67 per cent alcohol, and from such ribs, sections $3\frac{1}{2}\mu$ may be secured easily, giving a picture of bone marrow with its connective-tissue framework normally distended and marrow elements in normal position. On sections so thin an oil immersion objective may be used, blood stains employed, and eosinophilic cells in great numbers may be demonstrated outside the blood-vessels of the bone marrow. Particularly are these marrow elements, together with nucleated red blood corpuscles, shown with great beauty in the ribs of a 10-cm. embryo pig. Bone marrow in this form is a decidedly different tissue from bone marrow studied as a smear.

The thoracic wall of a small white rat, fixed by injection of Hermann's fluid, may be cut at $3\frac{1}{2}\mu$ without decalcification, and, stained with iron hematoxylin, shows not only marrow elements, but the intercostal muscles and nerves in normal position with the usual beauty of a Hermann's fluid fixation. In short, we get a penetration with Hermann's fluid impossible by the ordinary method of using it.

There is scarcely a tissue that is not shown with new beauty by this method of fixation. Sections of lung fixed by $HgCl_2$ injection and cut at $3\frac{1}{2}\mu$ give a picture unequalled in beauty. The epithelial lining is intact and shows the more perfectly in that the tissue is at normal distention.

A brain fixed and hardened in situ presents a very different appearance from a brain supported on a sheet of cotton.

The method is invaluable not only in preparing tissues for classes in histology, but also as a research method.

In the use of $HgCl_2$ as a fixer by the usual method, the crystalline deposits formed are very annoying and detract from the value of the fixer. This difficulty is overcome in the simplest manner. At a pressure 130 mm. mercury, 400 cc. of a saturated aqueous solution of $HgCl_2$ are injected in about 10 minutes into a small kitten or rabbit, the time depending somewhat on the freeness of the venous opening. If the venous opening is not sufficiently free an œdema is likely to be caused, which in some cases is no disadvantage. Follow the injection of the $HgCl_2$ by an injection of 500 cc. of 67 per cent alcohol. This not merely washes out the $HgCl_2$, but the $HgCl_2$ is about 3 times as soluble in alcohol of this strength as in water, so the washing out is doubly effective and the hardening of the tissue is begun at the same time. After such a washing out, if properly done, one may cut out whatever tissues desired without blackening the knife or tissues. It is usually best to leave the tissues in 67 per cent alcohol for one day, though, if necessary, they may be transferred at once to 82 per cent alcohol after having been washed out with 67 per cent alcohol.

It is found best to inject only one-half an animal at once. The canula should be placed in the abdominal aorta with the mouth just above the cœliac axis when injecting the thoracic viscera and head and neck, and low down in the thoracic aorta when injecting the abdominal viscera. In either case the vena cava should be opened either above or below the liver. It is best to place a block under the back of the animal to insure a free venous outflow.

If the animal is rare or valuable, a double canula may be placed in the abdominal aorta and the whole animal injected at once. After such an injection the whole animal, or the part injected may be left over night in 67 per cent alcohol and then removed to 82 per cent alcohol, which should be changed a few times. Thus a great deal of tissue, excellently prepared in a very short time, may be had on hand for any emergency.

The inner ear of a guinea pig fixed by $HgCl_2$ injection gives a rarely fine picture on section. After decalcification the cochlea should be laid open by a section passing through the modiolus. This permits better infiltration and imbedding, with the result that the delicate membranes are held in position by the celloidin when cut and do not present the appearance so often seen of having been dragged.

Tincture of iodine added to the 67 per cent alcohol used in washing out the $HgCl_2$ showed no noticeable advantage.

A very valuable use of the method is in the preserving of brain tissue. A brain may be fixed in situ by formalin injection, and then removed, the brain stem cut out and placed in potassium dichromate solutions preparatory to sectioning and staining by the Weigert-Pal method. Those who have had the disappointment of having such post-mortem changes take place in the inner capsule and pyramidal tracts, before the penetration of the fixer, as to render the tissue useless, will appreciate the value of this procedure.

Though many uses of the method have been noted they are but a part of the many ways in which the method was found very valuable in the Anatomical Laboratory of the Johns Hopkins University during the past year.

A CONVENIENT STILL TO MAKE ABSOLUTE ALCOHOL.

By William J. Calvert, M. D.,

Assistant Professor of Internal Medicine, University of Missouri.

In 1895, while working in the Anatomical Laboratory of the Johns Hopkins University, it occurred to me that the home manufacture of absolute alcohol would be more economical and satisfactory than buying it in small quantities. With permission from Dr. F. P. Mall, a small still was made which for a time gave satisfactory results. This apparatus consisted of an ordinary tin can and an inverted Liebig's condenser for the first portion of the work. When ready for distillation the condenser was changed to the inclined position and the alcohol was caught in an ordinary receiver. While this apparatus gave satisfactory results, it required more care and knowledge for its operation than can ordinarily be placed in an average janitor, already busy with numberless small chores. Since then, an absolute alcohol still has been constructed by Dr. Mall, which requires practically no care or thought on the part of the operator, yields an excellent quality of alcohol, and is inexpensive. The apparatus is made of heavy copper, tinned on the inside, and a block-tin worm. It is composed of a gas-stove, an automatic water-bath, boiler, condenser, and receiver. (Figs. 1 and 5.)

The only especial requisite for the gas-stove is a stop-cock in the supply pipe by which the gas flow may be regulated, thus permitting the stop-cock in the gas main to be turned on full. A stove similar to No. 8157, Eimer and Amend's Catalogue, 1902, p. 211, is satisfactory.

Naturally the size of the still must depend on the amount of work to be done. For making an amount of absolute alcohol used in our universities the following dimensions are sufficient: a water-bath, eleven inches in diameter and eleven and one-half inches high, with a substantial support one and one-half inches above its bottom to support the boiler and still, will allow one and one-half inches of water about the sides and bottom of a boiler eight inches in diameter and ten inches high. The support for the boiler should be fastened to the sides and bottom of the bath, with a small depression on the upper surface or several small uprights to hold the boiler in one place. The automatic water supply now used on the ordinary water-bath in chemical laboratories is sufficient. The connecting tube U should be three-fourths of an inch in diameter and not longer than one-fourth of an inch, placed four inches above the bottom of the bath. The tube V should be one inch in diameter, extend from a point level with top of bath to a point one inch below lower side of tube U, and be well anchored to side of water-bath, near the top. Supply tube X, Fig. 4, sufficiently large to take a one-half inch rubber tube, is inserted at a right angle into the posterior side of tube V two inches from top. One-fourth of an inch from tube V tube X is bent downward at an angle of 45°; this is to prevent kinking of rubber tube connecting X with C. The height of the water in V is regulated by height of tube W, which is either fastened in V by penetrating a cork stopper or permanently fixed in a cap to screw on V. Tube W should extend to one inch below top of V, and its lower end should accommodate a one-half inch rubber tube which carries waste water to a sink.

The boiler (Figs. 1 and 5) is eight inches in diameter

and ten inches high from bottom to side *Q*, which may slope inward and upward at any desired angle. The opening *P* to *P'* should be at least four inches; walls of neck *N* may be parallel or slightly flared at top and two inches high. At top of *N* a heavy flange *M* three-fourths of an inch wide is firmly attached. The top is composed of wall *O* which closely fits into neck *N* and extends about one-quarter of an inch below the point *P* and *P'*, with the lower edge slightly flanged inward as shown in the figure, to prevent, as far as possible, capillary attraction between the walls *O* and *N*. At the top of *O* a flange *L*, corresponding to flange *M*, is firmly attached, a sufficient distance above *M* to admit a rubber or asbestos ring. The top may then be firmly fastened to the boiler by placing

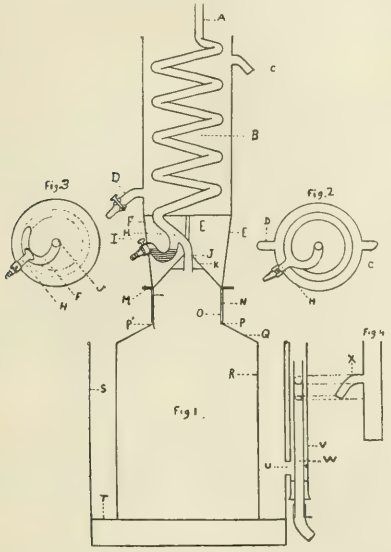


FIG. 1. Median section through the still.

FIG. 2 shows relative position between tube *H*, *D* and *C*. If the still is placed near or against a wall, tube *H* should be a little in front of the plane through *D* so that the cock *I* may be more easily reached.

FIG. 3 shows course of block-tin worm from bottom of condenser to *J* in Fig. 1, seen from below upward.

FIG. 4 is a side view of *V*, showing tube *X*.

several simple clamps on flanges. Beginning at top of *O*, the wall *K* extends upward, cone shaped, to an apex *J*, through which passes the lower end of the block-tin worm *A*. This joint will be more secure if the tin tube extends about one inch below the apex and is braced as shown in Fig. 1. Immediately above the point *J* the tin tube bends at almost a right angle and runs in a spiral direction outward and upward to the bottom of the condenser *B*, the bottom of which should be about one and one-half inches above the point *J*. The spiral tube is shown in Figs. 2 and 3. In the middle third of tube *F*, Fig. 3, is soldered a short piece of tin tubing, in which a stop-cock *I* is placed, in such a manner as to form a small trap in the bottom of tube *F*, which must be filled before the alcohol, returning from the condenser, can flow back to the boiler, Fig. 3. This trap is made by removing the bottom and spreading the sides of tube *F* to receive tube *H*. Tube *H*, in Fig. 3, contains a stop-cock, which, when closed, causes the return alcohol from the condenser to fill the trap and flow into the boiler and when open permits the return alcohol to flow through tube *H* to the absolute alcohol receiver. The lower end of tube *H* is to receive a three-eighths rubber tube, which in turn connects with a glass tube the lower end of which penetrates a cork in the absolute alcohol receiver, which is an ordinary large bottle.

The worm should be of one-half inch block-tin tubing, the coils of which should be from one and one-half to two inches

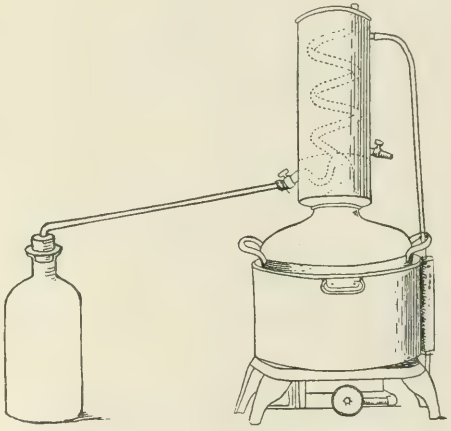


FIG. 5.—Side view of still, one-fourth scale.

apart and three-fourths of an inch from the walls of condenser *B*. When the coil reaches the top of condenser *B*, it should be deflected until the wall of the condenser is reached, here securely fastened and then extend perpendicularly upward four or five inches. Condenser *B* should be at least five inches in diameter and ten inches high, and firmly attached to top *K* by four supports, *E*, *E'*, *E''*. It is necessary to have condenser and top *K* one rigid piece to prevent straining the block-tin tube and disarranging the trap in tube *F*. Near the bottom of the condenser is a cold water intake *O*, for three-eighths rubber tubing, with stop-cock. On the opposite side one inch from top of condenser is an outflow pipe, *C*, for a one-half inch rubber tube. One-fourth of an inch from condenser, tubes *C* and *D* are deflected at 45° to prevent tubing from kinking. Across the top of condenser run two bars at right angles for supporting a handle to which is attached a rope which runs over a small pulley fixed in a bracket a few inches above the condenser. By means of this rope and pulley the condenser is raised so that the wall *O* of top clears wall *N*

of boiler and is then pushed to one side, so the boiler may be removed from the bath for cleaning and refilling. If the condenser is thus handled there is no danger of injuring the joint between *O* and *N*. The rubber tubing connecting the intake *D* with the water main and tube *C* with tube *X* must be sufficiently long to permit the condenser to swing free of the boiler.

The cheapest method of abstracting water from alcohol is by using fresh well burnt lime, quick lime according to the formula $CaO + H_2O = Ca(OH)_2$, which when expressed in atomic weight values is 55.85; 17.95 or 3.11 grams of quick lime for each gram of water. Ordinary commercial 95 per cent alcohol varies from 92 to 95 per cent alcohol, so contains from 5 to 8 grams of water per 100 cc. For safety it is best to calculate 5 grams of lime for each gram of water and allow for 10 cc. of water per 100 cc. of alcohol. On this basis it requires 500 grams of lime per liter or about four pounds of lime per gallon of alcohol.

Directions for operating the apparatus: The boiler is three-fourths filled with lime and 95 per cent alcohol, placed in the water bath, tightly connected with the condenser and allowed to stand over night. On the following morning the bath is heated to, and kept at, about 90° to 93° C. During the first two or three trials the stove must be regulated by the stop-cock in the gas stove, keeping the valve at the gas main open full. When the gas supply has been regulated the valve in stove must remain untouched. The supply of water is regulated by the valve at *D*, keeping the valve on the water main open full. In this way when the apparatus is to be used instructions are to put — grams or pounds of lime and — quarts of 95 per cent alcohol in boiler, tightly connect boiler and condenser, close valve *I*, allow to stand over night, in morning open water main valve and gas main valve full, light stove; in afternoon, shut off gas and water; next morning open water main and gas main valve full, light stove and open valve *I*. When alcohol ceases to flow into absolute alcohol receiver remove and tightly cork the absolute alcohol and immediately clean the boiler. If the lime is allowed to remain in boiler it may be difficult to remove.

Cost of absolute alcohol made in this way is about as follows. From 50 to 75 per cent of 95 per cent alcohol is recovered as absolute:

1 gallon absolute costs,	
2 gallons of 95 per cent, at 50 cents . . .	$1.00
8 lbs. of lime at from 3 to 4 cents	.24
About 100 ft. gas	.15
Water, about	.10
	$1.49

The cost in 95 per cent alcohol depends on the care in operating. If too much heat is used the loss will be greater. During the first day the alcohol need not boil, as a temperature near the boiling point will complete the reaction.

This still may also be used for making extracts, etc., and can be made of any desired capacity.

If the trap pictured in Fig. 3 be blown in a glass tube which could be connected with an ordinary Liebig's condenser a very convenient chemical apparatus would be had.

A number of these stills have been manufactured by Vaile and Young, 210 N. Calvert street, Baltimore, at a cost of about $25 each.

ANNOUNCEMENT CONCERNING GRADUATE INSTRUCTION IN THE MEDICAL DEPARTMENT OF THE JOHNS HOPKINS UNIVERSITY.

By W. H. Howell, M. D.,

Dean of the Medical Faculty.

The courses that have been offered to graduates in medicine by the Johns Hopkins University, since the opening of the Hospital in 1889, consisted in the beginning of a combination of general courses, laboratory and clinical, so arranged as to give systematic instruction to large groups of students. In recent years these courses have been given only during the months of May and June, and it has been found desirable to supplant the general courses, to a large extent, by special courses confined to a limited number of students. Although designated as graduate courses, the instruction has been for the most part of an elementary character, especially in the laboratory work, as many of those who entered had not enjoyed the advantages of a training in modern scientific methods. Our experience during the last few years, however, leads us to believe that at present there is no great need on the part of graduates for elementary courses of this character. The wide adoption of laboratory methods in all of our reputable medical colleges, and the general improvement in medical instruction that has been going on for a number of years past, have produced a better trained body of graduates, and those who desire to take post-graduate work are, as a rule, prepared for more special and advanced instruction. The Medical Faculty of the Johns Hopkins University believe, therefore, that the time has come to make specific provision for a higher grade of instruction to medical graduates. They have decided to abandon for the most part those systematic courses heretofore given in May and June, of which the chief aim was to supplement deficiencies in previous training. As a substitute for these May and June courses they propose to offer opportunities of a wider character which, while still

giving to those who so desire a chance to obtain elementary instruction, are especially intended to encourage the development of truly graduate work, such as can be accomplished most satisfactorily by individual study under competent direction. Specific regulations along these lines have been adopted and will be stated in full in the next annual announcement.

For the information of those who may desire to avail themselves of the facilities of the Medical School and the Hospital during the present session, it may be said that these regulations make possible the following opportunities:

1. In each department a limited number of graduates will be received during the whole or a part of the year, either to engage in advanced work of an individual character or to enter the regular courses given to undergraduates. Applications to enter upon such work should be made directly to the Head of the Department.

2. Each instructor in the Medical School may offer to graduates special courses in his subject at any time during the year. These courses may be similar to those heretofore offered during May and June only, that is, courses of a more or less elementary character, but limited to a small number of students so that personal supervision may be obtained from the instructor, or they may be arranged only for those who are prepared to do advanced work.

For the present the following courses may be announced. Those coming under the first group described are designated as University Courses, while those of shorter duration, coming under the second head, are designated as Special Courses. For further details, application may be made to the Dean of the Medical Department.

UNIVERSITY COURSES.

These courses are of two kinds, elementary and advanced. The elementary courses will cover the subject as usually given to undergraduates in medicine and the work may be done with the medical classes. The advanced courses will be given only to those who are prepared to undertake special studies, and the work will be done under the personal supervision of the instructor in charge of the course.

MEDICINE, *Elementary.* A limited number of physicians will be admitted to the regular class exercises in this subject, including ward rounds, clinics and work in the clinical laboratory. Fee $100.00 for the entire year; $50.00 for a half year. Applications should be made to Professor Osler.

MEDICINE, *Advanced.* Physicians properly trained in the methods of clinical diagnosis will be given opportunities for experimental investigation in the clinical laboratory. Fee $50.00 for the year. Applications should be made to Dr. C. P. Emerson.

GYNECOLOGICAL PATHOLOGY, *Elementary.* (Limited to three students.) Drs. Cullen and Hurdon.

The work in this course begins October 1 and extends to May 1. The class meets Tuesdays and Thursdays, 12 m. to 1 p. m. Fee $50.00. Applications for this course should be sent to Professor T. S. Cullen not later than September 15.

OBSTETRICS, *Advanced.* A limited number of physicians will be received for advanced instruction under Professor Williams during the Academic year—October to June. Those intending to enter upon this work should apply to Professor Williams stating the character of the work they desire and their qualifications for undertaking it. Fee $50.00

PATHOLOGY OF THE HEART AND CIRCULATORY SYSTEM, *Advanced.* (Limited to five students.) Professor W. G. MacCallum. The course will begin October 9 and continue for five weeks, with three exercises a week.

These exercises will consist of lectures, experiments on animals, and anatomical, chemical and microscopical demonstrations. The following topics will be considered: Diseases of the pericardium, diseases of the endocardium and myocardium, pathology of the pulmonary circulation, pathology of the systemic circulation, pathology of the lymphatic channels. Fee $30.00. Those desiring to take the course should correspond directly with Professor MacCallum.

PATHOLOGY, *Elementary.* A limited number of physicians will be received during the year in the courses in bacteriology and pathology. Fee for the entire year $50.00, fee for half year $25.00. Apply to Professor W. H. Welch.

PHARMACOLOGY AND TOXICOLOGY, *Elementary.* January 1 to June.

A limited number of physicians will be received into the regular course as outlined in the catalogue of the Medical School. Fee $25.00. Apply to Professor J. J. Abel.

PHARMACOLOGY AND TOXICOLOGY, *Advanced.* Professor Abel.

Those who have had the necessary preliminary training and who desire to do work of a special character will be received at any time during the Academic year. Fee $50.00 for the entire year.

PHYSIOLOGY, *Elementary.* (Limited to four.) Laboratory course in experimental physiology, October to December 25.

The work will consist in exercises in the various graphic methods used in physiology to study the properties of muscle and nerve and the circulatory and the respiratory organs. Fee $25.00. Apply to Professor W. H. Howell.

PHYSIOLOGY, *Advanced.* (Limited to two.) January to June 1. Professor Howell.

Individual instruction will be given in the methods used in physiological demonstrations and research. Especial attention will be paid to the methods employed in the study of the circulation. Fee $50.00.

ANATOMY, *Advanced.* Those who have had the necessary preliminary training and desire to undertake the study of special problems, will be received at any time during the Academic year. Fee $25.00. Apply to Professor F. P. Mall.

HISTOLOGY AND ORGANOLOGY, *Elementary.* Professor Harrison, Drs. Sabin and Knower, October 1 to February 15, Monday, Wednesday and Friday afternoons. (Limited to three.) Fee $50.00.

NEUROLOGY, *Elementary.* A systematic course in the gross and microscopic anatomy of the central nervous system, from February 1 to March 15. Lectures, Dr. Sabin, three hours a week; laboratory work, Dr. Sabin, Professor Harrison, Drs. Knower and Streeter, Monday, Wednesday and Friday afternoons. (Limited to five.) Fee $25.00.

NEUROLOGY, *Advanced.* (Limited to two.) Dr. Sabin, March 15 to June 1, forenoons.

The work will take up special topics in the development and structure of the central nervous system. Fee $25.00.

NEUROLOGICAL TECHNIQUE, *Advanced.* (Limited to two.) Dr. Streeter, March 15 to June 1. A knowledge of general histological technique will be assumed. Fee $25.00.

EMBRYOLOGY, *Elementary.* (Limited to two.) Dr. Knower, March 15 to June 1.

A laboratory course in the development of the mammalian body as illustrated by pig and human embryos. Fee $25.00.

HUMAN EMBRYOLOGY, *Advanced.* Professor F. P. Mall, October 1 to June 1. (Limited to two.) Fee $25.00.

EXPERIMENTAL EMBRYOLOGY, *Advanced and Research.* Professor Harrison, March 15 to June 1. (Limited to two.) Fee $25.00.

PHYSIOLOGICAL CHEMISTRY, *Elementary.* March 15 to June 1, every afternoon.

A limited number of physicians or others who have had the requisite preliminary training in chemistry will be received for the laboratory course and lectures given to the medical students. Fee $25.00. Apply to Professor Walter Jones.

PHYSIOLOGICAL CHEMISTRY, *Advanced.* Professors Abel and Jones.

Those who have the necessary preliminary training and who desire to do work of a special character will be received at any time during the Academic year. Fee $50.00, for the entire year.

SPECIAL COURSES.

MEDICINE. Drs. McCrae, Cole and Boggs, June 1 to July 1. (Limited to fifteen.) Fee $100.00.

The course will not be given if less than eight register. Applications for this course must be sent in not later than May 10.

The whole material of the medical service will be available for the class. Special attention will be given to the study of the general methods used in the clinic.

The course consists of:

I. *Ward Rounds.* Drs. McCrae and Cole, from 9 to 11 daily. Special attention will be given to diseases of the circulatory and digestive systems.

II. *Physical Diagnosis.* Dr. McCrae, five hours a week. The general methods of diagnosis will be taken up and special attention given to diseases of the thoracic and abdominal organs.

III. *Clinical Microscopy and Medical Bacteriology.* Dr. Boggs, three afternoons—9 hours a week. This course consists of lectures, demonstrations and especially of practical work. All of the available specimens of blood, urine, sputum, gastric contents and stools are studied. The ordinary methods of clinical bacteriology will be demonstrated.

PEDIATRICS. Dr. S. Amberg, June 1 to August 1, daily from 11 to 12, Dispensary. (Limited to eight.) Fee $40.00. The participants are expected to examine patients personally under supervision.

SURGICAL PATHOLOGY. Professor Bloodgood. This course is given three times during the year, as follows: Course I, October 10 to December 20; Course II, January 10 to April 20; Course III, May 2 to June 30. (Each course will be limited to twelve.) Fee $50.00.

The course consists of:

a. Systematic instruction in clinical and pathological diagnosis, illustrated by pamphlets, photographs, museum specimens, and microscopic sections.

b. Demonstrations on all fresh material received in the Surgical Pathological Laboratory.

Demonstrations, October to May, Tuesdays, 2:30 p. m. to 4:30 p. m.; Wednesdays and Fridays, 1:30 to 2:30 p. m. Demonstrations in May and June, Tuesdays, Thursdays and Fridays, 8 to 9 a. m. Students taking this course should plan to give at least three hours a day to the work.

OPERATIVE SURGERY ON ANIMALS. Professor Cushing, April 29 to June 21, Wednesdays and Saturdays. Sixteen exercises of from four to five hours each, commencing at 8:30 a. m. (Limited to ten.) Fee $60.00.

The course will be limited to ten graduate students who will be divided into two groups of five, thus making up two complete operating staffs, an operator, first and second assistant, anæsthetist, and attendant. The members of the class rotate in these positions during the various exercises. An effort is made to carry out as closely as possible the same technique that is used in the general operating room of the Hospital. The graduates taking the course do all of the operative work themselves.

Emphasis will be laid upon methods of operating in general, rather than upon any particular operations. A schedule of the exercises showing the operations performed will be furnished on application.

GENITO-URINARY SURGERY. Professor Young. Fee $100.00.

A limited number of graduates will be taken for special work in Genito-Urinary Surgery. The course will include clinical and laboratory work and the student is expected to give his entire time, or most of it, to the department, and to enter for six months or more. Research studies will be encouraged.

ORTHOPEDIC SURGERY. Dr. Baer, May 15 to August 1, Monday, Wednesday, Thursday and Saturday, 10 to 12 m. (Limited to ten.) Fee $50.00.

A course will be given in the Orthopedic Dispensary from 10 to 12 m. on the days noted in which the students will be given practical work in the diagnosis and treatment of all orthopedic affections. Ward rounds covering this class of cases will be made from 9 to 12 on Monday mornings. Opportunities at this and other hospitals will be posted during the course so that one may be able to see practically all orthopedic operations.

X-RAY DIAGNOSIS AND THERAPEUTICS. Dr. Baetjer. This course is given three times during the year as follows: Course I, October 15 to December 15; Course II, January 15 to March 15; Course III, April 15 to June 15. (Limited to five in each course.) Fee for each course, $50.00.

Each course will consist of daily demonstrations from 11 a. m. to 12:30 p. m., and the aim of the course is to give a practical knowledge of the construction of the X-Ray apparatus, and its use in diagnosis and treatment.

GYNECOLOGICAL PATHOLOGY. Professor Cullen, during March and April, Tuesday and Thursday, 12 to 1 p. m. Pathological Laboratory. (Limited to ten.) Fee $50.00.

A course in the diagnosis of uterine scrapings. All pathological conditions of the cervix and body of the uterus that could be mistaken for cancer are discussed, and special consideration is given to the early diagnosis of cancer of the uterus. The methods of obtaining and examining pieces of uterine tissue are given in detail.

CYSTOSCOPIC EXAMINATIONS. Dr. Hunner, Monday and Friday, 2 to 4 p. m. May 12 to July 30, inclusive. (Limited to six.) Fee $50.00.

Fifteen clinics covering the entire subject of diseases of the urinary tract in woman. Demonstrations of the newer instruments used in urinary work.

This course is for beginners in cystoscopy.

BACTERIOLOGY, *Elementary.* Dr. Ford, May 1 to June 1. Three mornings a week. (Limited to ten.) The character of the work will be adapted to the needs of the class. The course will include instruction in: 1. Elementary Bacteriology. 2. Sanitary Bacteriology, including water and milk. 3. Technique of agglutination, hæmolysis and immunization of smaller animals. Fee $50.00.

PATHOLOGY, *Elementary.* Dr. Bunting, May 1 to July 1. (Limited to ten.) Three afternoons a week. Lecture and laboratory exercises in general pathological histology.

The course will not be given if less than five register. Applications must be received before April 15. Fee $50.00.

OPHTHALMOSCOPY AND OPHTHALMOLOGY. Dr. Mills, June 1 to July 1, Monday, Wednesday and Friday, 3 to 4 p. m. (Limited to ten.) Fee $25.00.

This course is intended for general practitioners.

GROSS ANATOMY. Professor Lewis, October 1 to June 1, hours arranged with the instructor. Fee $25.00 per month.

Dissection, study of prepared specimens and of frozen sections.

REGISTRATION.

Before entering upon any of these courses of graduate instruction the student must register at the Office of the Dean of the Medical School. Upon payment of the requisite fees a card will be issued stating the courses which the holder is permitted to take. This card must be presented to the instructor in charge of each course at the beginning of the classwork in order that the holder may be duly recognized as a member of the class.

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Report on Typhoid Fever.

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CONTENTS.

PAGE

The Special Field of Neurological Surgery. By Harvey Cushing, M. D., ... 77

Tumor of the Parathyroid Gland. By W. G. MacCallum, M. D., . 87

Bacillus Violaceus Manilæ. By Paul G. Woolley, M. D., . . . 89

A Report Upon the Agglutination Reactions of the Bacillus Dysenteriæ (Shiga) with the Blood Serum of Patients Suffering with Summer Diarrhœa. By Charles K. Winne, Jr., M. D., . . 93

Repeated Copious Hæmoptysis from an Aortic Aneurism, Extending into the Right Lung and Finally Rupturing into the Pleura. By Thomas Wood Clarke, M. D., ... 98

A Case of Cæsarean Section Following Ventral Fixation. By Alfred Hull Clark, M. D., and Robert Lee Bowley, M. D., . . . 101

A Survey of Ovariotomy at Extremes of Life. Report of a Case in a Girl Aged 5. By Harry I. Wiel, ... 102

Proceedings of Societies:

The Johns Hopkins Hospital Medical Society, ... 109

Loss of Entire Lower Lip. Repair by Flap from the Arm [Dr. Watts];—Report of Cases: Adeno-carcinoma of the Umbilicus; Cancer of Liver; Melanotic Sarcoma with Metastases [Dr. Cullen];—Recurring Phlebitis of Obscure Origin [Dr. Briggs];—Demonstration of Pathological Specimens [Dr. MacCallum];—Biliary Cirrhosis of Family Type [Dr. Osler];—Crossed Dissociated Sensory Paralysis with Lesion of Medulla [Dr. Thomas];—Situs Transversus and Atresia of the Pylorus [Dr. Little and Mr. Helmholz];—Experimental Streptococcus Arthritis [Dr. Cole];—Professor Smith on the Jersey Mosquito [Dr. Kelly];—Gastric Ulcer: Clinical Varieties and Symptoms [Dr. Howard];—Gastric Ulcer: Diagnosis and Medical Treatment [Dr. McCrae];—Report of a Case of Ulcerative Endocarditis, with Embolism of the Aorta [Dr. Osler];—Case of Typhoid Fever Showing Some Unusual Features [Dr. Cole];—Puerperal Infection with Gas Bacillus [Dr. Little];—Report of a Case of Arteriovenous Aneurism of the Thigh [Dr. Osler];—Survey of Ovariotomy at Extremes of Life. Report of a Case in a Child aged Five [Mr. H. I. Wiel].

Notes on New Books, ... 120

THE SPECIAL FIELD OF NEUROLOGICAL SURGERY.[1]

By Harvey Cushing, M. D.,

Associate Professor of Surgery, The Johns Hopkins University.

Gentlemen:—In response to the friendly request of Dr. Crile, your presiding officer, I shall attempt to formulate some personal views concerning a branch of surgery, which, in this country at least, largely owing to the allurement of other and more immediately promising fields of operative endeavor, has hardly received the attention it deserves.

Through the generosity of Dr. Halsted, his junior associates have been given, in a measure, the privilege of directing the work in some of the subdivisions of his large surgical clinic, in order that they may concentrate their efforts toward advancement along particular lines. It has thus fallen to my lot, temporarily and under his guidance, to control the group of cases which present features chiefly of neurological interest; and it is upon the present possibilities and limitations, as well as upon the future outlook for this department of surgery, that I shall briefly dwell tonight.

To many of us as students, neurology was the *pons asinorum* of the medical curriculum. Nor can I recall any very earnest efforts to cross the bridge, particularly by those of us whose ability to visualize lesions, that probably had never been seen under the microscope nor handled in the gross, was—to say the least—not abnormally developed; and who, for the stimulation of their interest, needed certainties of diagnosis and assurances of therapeutic results. Even for a student, whose inclinations from the beginning may tend in this direction, a steady prosecution of the subject is beset with great discouragements. Special training is necessary before one can obtain a working knowledge of the underlying pathological processes, without which the clinical superstructure is built upon sand. The morbid anatomy of the lesions is greatly obscured by the imperfections of our methods of examination, but still more because they are but rarely seen except at the autopsy table and then only in their terminal stages. Furthermore, owing to the technical difficulties of our present laboratory methods, so long a time often elapses before the histological alterations in the tissues are demonstrable, that, in the interim, our recollection of the clinical picture has become dimmed and interest has fled elsewhere. That the morbid physiology of the subject—its experimental side—when compared with the researches that have been made in other directions, has hardly been touched, may be a matter of

[1] An Address delivered before the Academy of Medicine of Cleveland, November 18, 1904. Reprinted from the *Cleveland Medical Journal*, January, 1905.

regret, but can hardly surprise us when we consider that the normal structure and function of many parts of the nervous system remain as yet unknown. Finally, the privilege of regarding as historic the days when there existed "a plague of drugs least mischievous when merely superfluous," and which a century ago evoked the well-known aphorism of Benjamin Franklin—"He is the best physician who knows the worthlessness of the most medicines"—carries with it a satisfaction that is not without alloy. For what eager student of medicine can face without dismay the "poverty of therapy" that characterizes the present day, and which is emphasized more especially in the neurological clinic, which stands largely on the therapeutic tripod of iodine, bromine and electricity.

Will a more general application of surgical methods offer anything for this department in the way of diminishing the present number of the medicinally incurable, or of improving the condition of those whose maladies time alone, not medicine, restores to a certain degree? Certainly not, while the neurologist and surgeon maintain the same distant relations that have heretofore existed between them. Aware, so far as one who does not operate can be, of the possibilities of surgical therapy in a given condition, the neurologist spends days or weeks in working out the presumable location and nature of, let us say, a cerebral tumor. An operator is called in; he has little knowledge of maladies of this nature and less interest in them, but is willing to undertake the exploration. The supposed site of the growth is marked out for him on the scalp by the neurologist; and he proceeds to trephine. The dura is opened hesitatingly; the cortex is exposed, and too often no tumor is found. The operator's interest ceases with the exploration, and for the patient the common sequel is a hernia, a fungus cerebri, meningitis and death. But should this be a matter for surprise? Does the internist deem it his duty to instruct an operator in the mysteries of an abdominal tumor and show him where and how to make his exploration? Does he not demand that the surgeon should be as familiar with the symptomatology and the underlying morbid factors of the disease as he is himself? Certainly the relationship between the internist and the general surgeon is far closer than it was in the days of the professional herniotomist, whose instruments were looked over and who was directed in the course of his operation by the physician.

I take it that we all are, or should be, branches grown from the common stem of Medicine—in the broad Hippocratic meaning of the term—and nourished through the roots of General Pathology. And whether one chooses to follow lines of surgical therapy in his own subject, and another not, is purely a matter of personal inclination and manual training. Nor is it less true, I think, of any individual branch of this parent stem than of the tree itself, that, without flourishing surgical twigs, it will, like Dean Swift's noble elm, die at the top.[2]

But why this long preamble? Because it seems clear that in order to advance surgical measures, whether they are to deal with diseases of the nervous system, the deformities of children, the maladies peculiar to women, genito-urinary diseases, or those belonging to any other more or less limited branch, specialization, or better, concentration of thoughts and energies along given lines is necessary. Why are we so slow to understand that we cannot graft an independent twig of operative surgery on any of the branches of this huge medical tree and have it grow undeformed? Original growth from the main stem of general medicine and surgery is necessary, but some at least of those whose inclinations follow the branch of neurology, must do their own surgery, if it is to aid in the development of their therapy, and not depend on the help supplied by the lukewarm assistance of other departments.

To successfully cope with the many operative problems offered by the various disorders of the nervous system, a man, after a thorough training in pathology and medicine (in its broadest sense) must study, not only in the neurological clinic but also in the laboratory, the pathology of these afflictions in their histological and—what is still more important—in their experimental aspects. Any one who like myself has passed from general surgery into this special branch without this preliminary training, finds himself but ill prepared for his new work and must be satisfied to merely follow the lead of others, as I have largely had to do.

Though a surgeon possesses a natural tendency towards handicraft in matters therapeutic, I do not wish to be considered as one who distorts neurological problems by viewing them with an operative strabismus uncorrected by the proper spectacles. I wish merely, so far as my time allows, to point out some of the present possibilities of affording surgical relief in certain maladies for which the outlook is otherwise most forlorn, and at the same time to lay stress on certain points that give us hope for the future. I shall keep away, so far as possible, from beaten paths; for that a cerebral abscess should be evacuated, a ruptured meningeal vessel tied, the spinal cord relieved from pressure, and a severed nerve sutured, has long needed no comment.

The Brain and its Envelopes.

At the outset something may be said relative to the surgery of cerebral tumors. A very natural reaction followed after it became generally known how unsatisfactory had been the results in the early series of cases, so enthusiastically undertaken when for the first time aseptic processes had permitted surgeons to perform craniotomies with a certain assurance—so

[2] "The chief lesson of the Hippocratic period for us is that, in practice as in honor, medicine and surgery were then one; the Greek physician had no more scruple in using his hands in the service of his brains than had Phidias or Archimedes; and it was by this co-operation in the fifth century that the advance was achieved which in our eyes is marvellous. As we pursue the history of medicine in later times we shall see the error, the blindness, and the vanity of physicians who neglected and despised a noble handicraft. The clear eyes of the ancient Greeks perceived that an art is not liberal or illiberal by its manipulations, but by its ends."—Clifford Allbutt. An Address on the Historical Relations between Surgery and Medicine. The Congress of Arts and Sciences, St. Louis, Sept. 27, 1904.

far as wound healing was concerned—of operative safety. In 1891, Agnew concluded an admirable paper on the subject with the words, "it is more than probable that, as our observations multiply, the sphere of the trephine, as a preliminary measure for the removal of brain tumors, will be lessened rather than amplified." And this from the city which, perhaps above all others, has since contributed the greatest number of successful cases! Von Bergmann's discouraging views are too well known to repeat here, and I doubt not that his opinion has done more than any other single factor to keep the surgery of this particular group of cases at a standstill: just as the views of the physiologist Flourens—that all parts of the cortex have precisely the same signification—so long retarded the studies of cerebral localization. Happily for us things are far different today. Not only has the localization of the more approachable parts of the cortex—after a long series of researches culminating in Flechsig's anatomical observations [3] and in the experimental researches of Sherrington and his co-workers,[4]—been put on a working basis for us, but also through the enormous strides in operative technique, particularly through Wagner's osteoplastic method of resection, we are now able to bring under observation extensive portions of the cerebral surface. In the earlier days of cranial surgery, it must be remembered, lesions in the motor area of the cortex were about the only ones that were considered approachable, and when we realize how far afield the experimentalists had gone in delimiting the "motor cortex" and, guided solely by calculations of the Rolandic area made upon the scalp, through what small trephine openings operators attempted to disclose underlying growths, it is little wonder that failures were almost universal. Today the reports of successful extirpations [5] are becoming more and more frequent.

Happily also a perfect functional restoration has taken place in many cases, for we now know that a considerable percentage of the growths originate in the meninges and, being by nature non-infiltrating, damage the cerebrum by a compressive invasion alone.

It is, however, upon another and less thoroughly ventilated aspect of the subject that I wish to dwell, namely upon the performance of palliative operations both for the supposedly inaccessible growths as well as for those which in the light of our present knowledge still remain non-localizable. In affording a measure of relief to these distressing cases, one may fulfill the chief of his duties as a physician—to prolong life and at the same time alleviate suffering. For the mere lengthening of a patient's months or years without rendering them more livable, is, as Dr. Fitz has so emphatically pointed out, no justification whatsoever of an operative procedure.[6]

The triad of symptoms, the profound headache, the vomiting, and sooner or later the stasis papillæ with ensuing loss of vision, are due to the increased tension and consequent disturbance of circulation within the closed box of the skull. Whatever and wherever be the lesion itself—whether there be a simple growth located in a hemisphere, another which obstructs in some way the outflow of cerebro-spinal fluid, a ventricular dilatation from inflammatory causes, or circulatory disturbances from a longitudinal sinus thrombosis—in all cases the tension phenomena are the same, varying only in degree and in their time of onset. The symptoms of a localizing nature whether motor, sensory, visual, psychic,[7] or what not, that may be superimposed on this triad, bear no necessary relation to the headache, vomiting and ocular symptoms, which, if unrelieved, cause perpetual suffering, lead to blindness, and finally are responsible for death itself, except in those rare instances of direct implication of some vital center in a spreading lesion. Complete relief to these symptoms may be brought about, and brought about promptly, in the vast majority of cases by the "decompression" of a palliative cranicctomy as many neurologists [8] and surgeons have emphasized, and patients may go on for months or possibly years, free from pain, and best of all, with their eyesight preserved.

I have at the present time several of these cases under observation, patients who before the operation were bed-ridden and suffering invalids. Two of them have been able to return to their occupations; some others, sad to relate, though comfortable, are practically blind owing to the long postponement of the decompression. And it is for the preservation of vision, particularly in these cases in which the intellectual faculties are in no way disturbed, that the operation should be resorted

[3] Paul Flechsig, "Einige Bemerkungen über die Untersuchungsmethoden der Grosshirnrinde, insbesondere des Menschen." Berichten der mathematisch-physischen Klasse der Königl. Sächs. Gesellschaft der Wissenschaften zu Leipzig. Sitzung vom 11 Jan., 1904.

[4] Grünbaum and Sherrington. The Cerebral Cortex of the Higher Apes. Proceedings of the Royal Soc., 1901.

[5] Even of growths from situations, which a few years ago were considered inaccessible; such as the "lateral-recess," tumors (cerebello-pontine), of which Sir Victor Horsley has had a considerable series. It is not impossible that a diseased pituitary body may some day be successfully attacked.

[6] R. H. Fitz. Some Surgical Tendencies from a Medical Point of View. Boston Medical and Surgical Journal, Vol. 145, Dec. 19, 1901.

"Any operation which does not better the condition of the patient must be regarded as a therapeutic error, since the knowledge thus obtained shows that the operation should not have been performed."

[7] The cases with superimposed psychic symptoms, indicating as they do lesions of the frontal lobes, frequently end their days in asylums for the insane. The recent report by Blackburn ("Intracranial Tumors among the Insane," 1903, Gov. Printing Office, Washington) from the Government Hospital for the Insane, records the discovery, in their series of autopsies, of 28 true tumors, of which 17 were of the so-called "endothelial sarcoma" variety; that is, they were comparatively benign growths, originating from the meninges and many of them distinctly operable.

[8] Thus Alfred Sänger of Hamburg, in a paper (Ueber die Palliativ-operation des Schädels bei inoperablen Hirntumoren) read before the German Surgical Congress, says: "In short, palliative trepanation in case of cerebral tumor is an operation which even if not absolutely free from danger, is of extraordinary blessedness, and, in the hands of a practiced surgeon, one that I would like to recommend in every case, in consideration of the impotency of internal medicine and in view of the distressful (qualvollen) suffering, and above all of the menacing blindness."

to promptly, that is, as early as possible after the diagnosis of probable brain tumor has been made.

The dread of the operating room, which many doctors share with their patients, together with the supposed uncertainties of an exploration, has led and still leads to one invariable course of treatment, large doses of the iodides being given with the vague hope that lues venerea may be at the bottom of the trouble. But even should there be definite grounds for this suspicion, the indications for an operation in many cases are none the less clear. In the first place, many, perhaps the largest proportion, of the gummata are superficial, accessible, and when exposed easily enucleated: they are, furthermore, very resistant to the usual antisyphilitic therapy, and, during the necessarily long term of treatment, the experience of watching a choked disc going on to a more or less complete optic atrophy, or of seeing other troubles supervene, is by no means uncommon. Some time ago I had under my care a patient, known to have had syphilis, and who presented symptoms of a cerebral growth, presumably an approachable one, since irritative motor phenomena of a Jacksonian character were superimposed. It was deemed advisable, on consultation, to prolong still further the use of mercury and potassium iodide, though these drugs had already been given a fair trial, with only a modicum of relief. The woman died suddenly one night in status epilepticus and at the autopsy a cortical gumma was found in the situation expected. Such experiences should teach us that, unless the intracranial symptoms, in cases of this sort, subside very rapidly under the treatment, a more prolonged trial of these drugs had better be reserved for the post-operative period. Moreover it must not be forgotten that symptoms occasioned by non-luetic processes, often for a time show a marked amelioration under these every-day measures, so that, unless we are on our guard, we may easily be led astray in our conclusions based upon these so-called therapeutic aids to diagnosis.

A palliative trepanation, although in itself not a very difficult operation, demands not a little forethought as well as manipulative skill. When there is no expectation of finding a growth and when the operation is to be carried out for decompressive purposes only, the site must be carefully chosen, for the hernia which necessarily results, and which is meant to act as a "safety valve" for the compressed brain, strangulates practically all function out of that portion of the cerebrum which protrudes. For this reason we must be careful lest, in relieving the patient of his pain, we substitute some serious form of paralysis. A more or less silent field of the cortex, therefore, should be selected. A relatively wide area of bone must be removed, its extent depending upon the degree of tension found at operation. The dura should be left open, after being slit up in a stellate fashion to the edge of the wound, or better still cut away entirely; otherwise there may be local pain resulting from pressure by the hernia which may crowd this sensitive membrane against the edge of the bone. Even to the painstaking final approximation of the scalp wound, every detail of the operation and of the local after-treatment must be followed out with the greatest care, if one wishes to avoid that most distressing of all complications, a fungus cerebri, which I am happy to say has occurred to me only twice in a long series of operations. In some cases of "silent" basilar tumors leading to an obstruction of the ventricular outflow the herniæ have rapidly grown to be almost as large as the patient's head without any parting of the scar.[9]

The particular form of decompressive operation which has proved most serviceable in the majority of the recent cases of non-localizable growths, is an inter-muscular one, sometimes conducted bilaterally, through the temporal region, with the removal of the squamous portion of the os temporale and closure of the muscle and its fascia over the denuded brain. But of the details of this procedure, more will be said in another paper.

I shall now pass on to the consideration of another large group of cases, those in which the symptoms are due to intracranial hemorrhage. Certain of these, more particularly the extradural forms of circumscribed effusion, which are usually due to the laceration of a branch of the meningeal artery, have long been recognized as distinctly and urgently operable. Interference with other varieties of hemorrhage is less commonly advocated. Nevertheless, we are coming to feel that the diffuse subdural hemorrhage associated with fracture of the base of the skull, the hemorrhage which occurs in the newborn—both of which usually follow the rupture of veins alone—and also the arterial hemorrhages of the adult into the substance of the brain, in selected cases, are as properly and advisedly attacked surgically as are the more accessible, localizable, and easily treated effusions of the blood.

In the diffuse bleeding from traumatic basal fractures, which in most cases can readily be differentiated from the extradural form by means of a lumbar puncture, there often is urgent need for decompression with the evacuation of clots, and drainage, if there is a continuance of the bleeding. In these cases also, the operation mentioned above has been found to be the most convenient means of approach. Of course it is not always possible to save these patients when the extravasation is large and especially when it is associated with a serious contusion of the brain. Nevertheless, trepanation will go a long way toward warding off the later compression effects produced by traumatic œdema, which, in the light of Cannon's experiments, is doubtless responsible for many of the fatalities.

Some months ago during a race, two young men were thrown from a tandem motor-cycle, and both sustained severe cranial injuries. They were brought to the hospital, unconscious. Bloody fluid was withdrawn from the lumbar subarachnoid space of each patient. One of them, apparently the more severely injured, was trephined low down in the skull, and bloody fluid with clots in considerable amount was evac-

[9] Many of the technical details, found to be best adapted to my personal needs in performing cranial operations, and in avoiding local post-operative complications, have been described elsewhere. (Pneumatic Tourniquets, etc. The Medical News, March 26, 1904.)

uated; the other was left alone. The former patient was up in 48 hours, after the operation; he was entirely free from symptoms, left the hospital early, and would probably have been well, today, had he not a short time later died the almost inevitable traumatic death of a motor-cycle pace-maker. The other patient remained in the hospital for a month, during which time he complained of headache, dizziness and the usual familiar sequels of these injuries, from which he has never become entirely free.

To cite a second case: A young man was tilted out of the back seat of a wagon by the unexpected starting of the vehicle, and landed upon the back of his head on the hard road. After some hours of unconsciousness he was found to have a homonymous hemianopsia and aphasia. Instead of investigating the cause of these symptoms, presumably due to local hemorrhages in the right occipital lobe, and, by contrecoup, in the left inferior frontal region, his physician, owing to the fact that there was neither a scalp wound nor any external evidence of fracture, and because the patient was making a progressive though slow improvement, decided against operation. Two months later there occurred an epileptic attack with a peculiar uncontrollable motor-speech (jargon) aura. These attacks increased in frequency and severity. Finally, a year later, the lower frontal convolutions were exposed, disclosing an adherent dura and a depressed scar over Broca's convolution. The epileptic attacks have ceased, but the visual defect and aphasia remain as before.

In the following case a different course was followed: A college boy sustained a severe blow on the head during a football scrimmage, and soon became unconscious. There was no indication of any external lesion. Though his symptoms had in large part subsided by the following day, he remained somewhat stuporous, responding slowly and reluctantly to inquiries. The movements of the face, tongue and arm on the right side seemed somewhat less free than those of the corresponding parts on the opposite side, and when roused and questioned, the patient stated that his hand was "numb." Blood-stained fluid was found within the lumbar meninges. Through an intermuscular incision in the left temporal region a subdural clot, about a centimeter thick and covering the lower Rolandic area, was bluntly scraped and irrigated away. The patient came out of the anæsthetic with a perfectly clear and active sensorium, though with no memory of the events subsequent to the injury. His convalescence was rapid and he escaped the usual slow restoration to the normal—perhaps never quite to the normal—of these cases when left alone. Numerous other instances might be enumerated.

For the more severe, the more desperately injured cases, which present bulbar symptoms, owing to an implication of the vaso-motor, vagus and respiratory centers, a prompt craniotomy, perhaps bilateral and into the cerebellar fossa, with evacuation of clots and drainage, offers the only hope of life. In passing, I may remind you that it is clinically well recognized that when these intracranial hemorrhages are complicated by extensive fractures of the cranial vault, the patients more frequently fail to show critical symptoms than do those who have escaped with an intact though fissured skull.

Much more important, it seems to me, are the intracranial hemorrhages which occur at birth. The problem is the same as in the cases just mentioned, there being a free escape of venous blood into the subarachnoid space, but with the additional element in favor of the child that the cranium is in a measure distensible. The conditions, therefore, are comparable to those hinted at above as occurring in the adult, namely a diffuse hemorrhage accompanied by some fragmentation of the vault. But given the distensibility of the cranium, the immediate consequences are not so likely to be serious even with an extensive effusion; and yet the late sequels are lamentable enough. The usual history is sadly familiar to all of us: A first-born child; a prolonged labor, often ending with instrumental delivery; some difficulty experienced in getting the child to breathe satisfactorily; a tense fontanelle; the child too weak to suckle and so fed by a dropper for several days; and after a time an apparent restoration to health. But too often, some months later, it is noticed that the child uses one side of the body, an arm or a leg, badly, or may be mentally deficient or blind. He eventually grows up, often with one or more spastic limbs, but worst of all, not uncommonly, he is subject to cortical fits. In this particular group of epileptics I have had a considerable experience in trephining and when the attacks were of a Jacksonian (motor) character, in extirpating areas of the precentral gyrus. And I can only say that the extraordinary variety of cortical lesions encountered defies description. Why should not these children at the time of the accident have been afforded the same chance of avoiding subsequent complications that is given an adult with intracranial hemorrhage? The reason is not far to seek. The author of one of our best text-books of neurology accredits most of the cases of spastic paraplegia to hemorrhages occurring at birth or in infancy, and while granting that it would be ideal if we could, at the time, treat them surgically, concludes that infants could not possibly survive the ordeal. A leading pædiatrist, also, whose knowledge of the pathology and symptomatology of these conditions is surpassed by none, has stated that these lesions cannot be attacked at the time of their occurrence because the coagulation time of the blood in the new-born is so slow that a fatal hemorrhage would necessarily follow any operation of this severity. This latter view would seem to have resulted from a misconception, unless our observations on coagulation are at fault; and, so far as endurance of the operative procedure is concerned, when one considers what the child's head is fitted by nature to withstand during parturition, the far milder traumatism of an operative procedure should on *a priori* grounds certainly be as well borne.

Two years ago, while making some investigations on the cerebro-spinal space, I was privileged by the obstetrical department to autopsy a number of the children, who were stillborn or who had survived only a few hours or days. To my surprise I found that about half of them had died with, if not

from, an intracranial hemorrhage.[10] Shortly after this Dr. Dabney consulted me in regard to an infant, 48 hours old, the first born of twins, which evidently was dying with compression symptoms. Contrasted with its normal twin the child had a very tense fontanelle, a slow pulse, slow and irregular respiration and a dilated right pupil. We operated as soon as preparations could be made. The right parietal bone was turned down and on opening the tense, plum-colored dura there was found a large, thick clot, which spread over almost the entire hemisphere. This was easily broken up and irrigated away with warm salt solution and the wound was closed. The child survived only eight hours. Since that time, however, I have had two successful operations of a similar nature, the details of which need not be entered into here except to say that preservation of warmth and avoidance of loss of blood may be regarded as the prime essentials. The procedure itself, though delicate in performance, need not entail serious consequences. In the last case a bilateral operation was performed, in order to expose both hemispheres.

The third group of hemorrhages, of which a word will be said, is of a totally different variety, being arterial in origin and intracerebral in site. Nevertheless, I am convinced that in properly selected instances much may be accomplished for these cases also, by proper operative intervention. The lesion by nature is, of course, an immediately destructive one and cannot be obviated by an evacuation of the clot; still it probably lies in our power to effectually ward off the fatality, which results from an exhaustion of the medullary centers, subjected, over a prolonged period, to an increased tension of high degree. The damage already done to the brain, however, particularly by a hemorrhage in the right hemisphere, is not necessarily incompatible with subsequent physical and mental activities of a high order.

None of the cases of apoplexy upon which I have operated, have recovered; improvement, however, after the trepanation was considerable in all of them in spite of the fact that only those patients were subjected to the operation, who, at the time, were profoundly unconscious and for whom death seemed imminent. For two or three days the condition of one of them was so much better that hopes of recovery were entertained; but he succumbed, apparently from an inhalation pneumonia. In view of the fact that no anæsthetic had been necessary, we can only suppose that the pulmonary complication had originated during the long period of snoring and irregular (Cheyne-Stokes) respiration, that had preceded the operation.[11]

The exploration could be done much better today, I think, by employing the intermuscular operation through the temporal region to which reference has been made. Anyone who has had the experience of opening the skull and dura in a case of apoplexy and consequently is aware of the enormous degree of cerebral tension encountered, would hesitate to expose the brain in another, similar case, unless safeguarded by an intermuscular means of approach. Fortunately, the temporal region furnishes the nearest access to the usual large capsular clot; and according to my experience, when a sufficient opening has been made down to it, the clot will practically extrude itself.

The only case of actual intracerebral hemorrhage which I have seen recover after operation was in a patient from Dr. Thomas' clinic in whom the bleeding had followed a penetrating stab-wound of the left superior parietal region. This had produced an extensive contra-lateral hemianæsthesia, astereognosis, loss of muscle sense and word blindness. At the operation the cortex was incised in the track of the puncture and on reaching the hemorrhagic cavity, clots, amounting to about an ounce, extruded themselves with immediate subsidence of the increased tension. This patient still retains some blunting of stereognostic perception in the right hand; but all of the other sensory symptoms disappeared within a few days after the operation.

There are many other intracranial conditions that promise to have an essentially operative therapy when our knowledge of the underlying mechanical conditions has been increased. As one example may be mentioned internal hydrocephalus with its oft accompanying maldevelopment of the spine—a condition which hitherto has successfully baffled all efforts to secure satisfactory remedial measures. In the series of cases (now six in all) observed during the past few years at the Johns Hopkins Hospital and in which drainage into the retroperitoneal space by trephining the vertebra, has been carried out, it seems that the nearest approach to a rational operation has been attempted, and the results in three of the cases have been most encouraging. But it is necessary before going any farther, to learn something more of the mechanical factors which lead to the condition, by further experimental study of the normal course of the circulation of the cerebro-spinal fluid, and if possible, by the experimental production of these anomalies in the lower animals.

Similarly, drainage of the meningeal spaces, when they are infected, is by no means a hopeless surgical problem, although much is to be learned by experience of ways and means to this end. One patient that was operated upon some years ago, for a purulent (staphylococcus aureus) spinal lepto-meningitis, after irrigation and prolonged drainage, entirely recovered from the local infection. His death occurred six months later from the complications of a pyo-nephrosis and at the autopsy, beyond the slight scar in the dura, Dr. Flexner could observe no macroscopical evidence whatever of any preexisting infection.[12] In the epidemic forms of meningitis, though a few cases presenting serious compression phenomena, have

[10] The lesion frequently found was a rupture of one of the delicate cerebral veins near its point of entry into the longitudinal sinus, the vessel having been torn, doubtless, by the strain put upon it from the overlapping of the parietal bones during labor.

[11] From a physiological point of view, reference has already been made to these cases in the American Journal of the Medical Sciences for June, 1903. "The Blood-pressure Reaction of Acute Cerebral Compression," etc.

[12] This case, among others, was reported by Dr. Osler in the Cavendish Lecture, June 24, 1899.

been surgically drained and irrigated in one way or another, no permanent beneficial effects have been observed, though the symptoms frequently abate in great measure and life may seemingly be prolonged, much as by the use of frequent lumbar punctures. Similarly in one child with hemorrhagic encephalitis, the threatened terminal symptoms of the paralytic stage were warded off by a decompressive operation, but without anything more than a postponement of the eventual fatality. It is not impossible that in the slowly progressive infections of a tuberculous origin, the mere exposure of the meninges may exercise some beneficial effect, as seems to be the case in tuberculous peritonitis, by increasing the local resistance of the tissues to the spread of the disease.

Maladies, such, for example, as the major neuralgias of the trigeminus and the complications of suppurative otitis media have belonged too long to the field of surgery to need any detailed mention here. But before leaving the subject of operations upon the brain, however, I should like to say something in general of methods of procedure.

Chloroform narcosis has been advocated by the highest authority, for the reason that less bleeding accompanies operations under its administration than when ether is employed.

This is undoubtedly true, but this result is brought about through the lowering of blood pressure, the very condition that one would wish to avoid and one, which, were it desirable, could readily be assured by a certain amount of blood-letting. Ether is a much safer drug.[18] The only annoying arterial hemorrhage comes from the scalp and in the majority of craniotomies (all but basal ones) this may be controlled by the proper use of a tourniquet. The venous hemorrhage, which at times may be profuse, from the diploe, sinuses or brain, must be controlled by special methods. Posture is oftentimes of great help in lessening this form of bleeding, but an upright position is attended by some hazard unless some means of supporting the general arterial pressure is employed. In this connection the inflatable suit, the result of the ingenious researches of Dr. Crile, can often be used to advantage. With our present knowledge the doctrine that in cranial operations rapidity is all-important would certainly appear to be based upon erroneous conceptions. I feel sure that experience will show that in cranial work, as in operations elsewhere, time, in the majority of cases, is vastly secondary in importance to careful hæmostasis.

The Spinal Cord.

The surgical procedures, which we are called upon to carry out for spinal lesions, require no such delicacy of handicraftmanship, and present no such critical complications as those with which we have just been dealing. For purposes of localization, however, a knowledge of neurological anatomy is no less essential for work here than on the brain, and the site of each segmental unit in relation to the skeletal landmarks must be familiarized, as well as the physiological part which each of them plays. There are no clinical puzzles more interesting to disentangle, none more confusing when left in a snarl, than those connected with the segmental localization of a cord lesion; the determination from disturbances of function of its transverse extent; a decision as to the recoverability of the injured tracts; and a knowledge of just where the intact arches of the spinal vertebra must be entered in order to expose the diseased focus. The small and removable spinal cord tumors especially put one's knowledge of localization to the test. The primary growths fortunately, are usually of a benign nature; they spring from the meninges, are enucleable, and if removed early allow of complete restoration of function in the cord. Probably these meningeal (intrathecal) tumors are by no means rare, and that so few successful extirpations have been recorded in this country, is possibly due to the fact that mistaken diagnoses have been frequent, explorations have been lamentably rare, and too often localizations have been incorrectly made. A single visit to the laboratory of the Queen's Square Hospital and a view of the tumors of this nature there preserved, enables one to realize how frequently in other parts of the world they must have been overlooked.

My personal experience with spinal tumors has been small. I have had one successful case of an enucleable tumor, with complete and early recovery from the compression paralyses. In another patient, who had been treated for 17 years for transverse myelitis, a fibroma was found, the size of a man's fist, which had caused a compression erosion of the overlying vertebra. At so late a date the cord had naturally been destroyed beyond repair. In a third patient, a child, the pressure of a mid-dorsal, inclusion (dermoid) cyst had caused symptoms of a total physiological transverse lesion; a complete restoration of function has followed its removal. The other cases have been illustrations simply of invasion of the spinal canal from without, usually by malignant disease. One of these patients almost completely recovered from the compression symptoms after a laminectomy and the removal of as much of the growth as was accessible. Some months later the pressure symptoms returned with accompanying severe root pains and a second operation was undertaken and abandoned as hopeless. Had I appreciated the intensity of suffering which this patient was destined to undergo, purely as a palliative measure I would deliberately have divided the cord at a point a segment or two above the growth. I believe this to be a justifiable measure whenever disease of a hopeless character has seriously damaged the cord and when the radiating root pains are severe.

The indications for surgical intervention in cases of spinal traumatism when there is evidence of injury to the cord, have given rise to much discussion. On the Baconian principle that "it is easier to evolve truth from possible error than from certain confusion" and for the sake of having some tangible

[18] The effect of the anæsthetic, together with other physiological reactions, reflex and otherwise, associated with operations upon the central nervous system, is best appreciated by keeping a blood-pressure chart. Such a record not only furnishes instructive and interesting general data, but often furnishes a means of properly interpreting the effects, beneficial or otherwise, of the various operative steps.

and definite rule for conduct, I have always divided these cases into three categories. (1) Those in which an operation is contraindicated because it can do no good and may increase the damage already done. To this group belongs the traumatic hæmatomyelias, a not uncommon lesion, one easily recognized from its symptoms alone and without radiographic aid, and one which, up to a certain point is recoverable by natural processes of repair. Of these cases we have had twelve. (2) Cases of fracture-dislocation, which are relatively common and which, so far as we know, are beyond all hope of restoration, owing to the complete transverse nature of the lesion. In these, operation can do no harm, but it is an unjustifiable ordeal for both patient and operator. (3) Cases of partial injury to the cord with symptoms which are increased and perpetuated by pressure from a foreign body, such as a fragment of bone or a bullet, form a group in which an operation undoubtedly will do good, provided it is so conducted as not to aggravate by further traumatism the already existing symptoms. All of these conditions are commonly regarded as surgical, and I have mentioned them for the sake of emphasizing certain limitations which should be recognized. Not a few cases of hæmatomyelia have come under my notice in which the symptoms were markedly aggravated by surgical meddling, and I have known many cases of total transverse lesion which have been needlessly subjected to laminectomy.

I do not hesitate to confess that elements of error may be present in this working division. For it is possible that certain cases of focal hemorrhage into the substance of the cord, like similar conditions in the brain, may come to be considered surgical disorders. Again we are not in a position to say with finality, that divided spinal tracts are incapable of regeneration; nor can we always be certain that a complete transverse destruction of a segment and not a partial injury with a physiological "block" of the remainder is indicated by the disturbances of function caudad to a lesion. Undoubtedly either of these conditions might give rise to an immediate total flaccid paralysis, an absolute anæsthesia up to its segmental level, a total and permanent loss of the deep, and a progressive diminution and final loss of the superficial reflexes. Collier's recent studies [14] offer strong evidence in favor of some regenerative power of the conducting paths, and they show furthermore, that the supposed symptoms of an anatomically total lesion are not unequivocal. If this assumption proves to be true, even the cases falling into my second group become as urgently operable as any, inasmuch as "the onset of the flaccid state in compression paraplegia is a sign which indicates that operative interference for the relief of pressure must be undertaken at once, if it is to be of any avail; for the total physiological abrogation from compression signifies the presence of serious evascularization, and the inevitable sequel of such ischæmia—irreparable degeneration—cannot long be delayed."

Only in the long-standing cases, therefore, which present when seen undoubted evidences of transverse destruction—no matter whether the lesion in its transverse extent originally was or was not complete—is an operation to be considered utterly futile. But though a laminectomy may avail nothing, much may be done in a palliative way even for these hopeless cases. Most important is the care of the bladder and in view of the functional isolation of the lower sacral segments, it is a wise routine practice to institute permanent drainage by a perineal or a suprapubic cystostomy. The procedure is a simple one, indeed not even requiring a local anæsthetic, for in low level lesions the perineal operation may be carried out, and, providing the cord injury be above the twelfth thoracic segment, the suprapubic route may be chosen. From either the gain to the patient in comfort and tidiness, and to the attendant in freedom from responsibility is immeasurable. Nothing is so provocative of pressure decubitus as the maceration of the skin from a dribbling bladder, and nothing so inevitably follows frequent catheterization as a terminal infection.

Did the scope of this address permit, many other problems connected with the surgery of the spine might be considered, for example: Under what circumstances should the pressure palsies following a tuberculous spondylitis be treated by the open method? What may we expect from sensory root division or excision of the dorsal root ganglia in the intractable neuralgias which may follow amputations or herpes zoster? What diagnostic value is to be attached to the measurement of tension as well as to the cellular content and chemical composition of the cerebro-spinal fluid obtained by lumbar puncture? What of the administration of medicaments by this route and for what physiological reason has spinal anæsthetization by cocaine fallen into disgrace? The discussion of these questions must be left for another occasion.

The Peripheral Nerves.

Of the many comparatively new discoveries that have a practical bearing upon the surgery of the peripheral nervous system, both somatic and splanchnic, much could be said, both in regard to the successes as well as in explanation of the failures in this more familiar field of neurological surgery. At present I must content myself with the brief presentation of some few of them.

The process of repair, that precedes the restoration of function in injured and degenerated nerves, represents the key to the situation. This must be found before the last word on nerve suture and nerve anastomosis can be said. Some of the most important and suggestive pieces of scientific investigation of recent years have been directed toward the solution of this problem, and, although the question is not yet ended, many of the facts, which have been brought to light during its course, have proven of clinical importance through their practical applicability. The doctrine, commonly accredited to His, that each nerve fiber is an outgrowth of a single cell, the two making a nerve unit, for a long time met with almost universal acceptance. More recently, however, strong opposition against this view has developed owing to the studies of Bethe, Nissl,

[14] Collier, The Effects of Total Transverse Lesion of the spinal cord in Man. Brain, 1904, Vol. 27, p. 38.

Dohrn, Schultze and others, who claim that the fibers do not grow out from the central nerve cells, but arise independently in the periphery from chains of cells which ultimately represent the sheath of Schwann and which only secondarily become united with the central cell. If this view proves to be correct, and if the histological and functional changes, which Huber and Howell, Bethe, Ballance and Stewart, and many others, have observed to take place in the peripheral end of a divided nerve, without any discoverable reunion with its central end, prove actually to be regenerative processes of the nerve, the possibilities of future work on the peripheral nerves promise to be enormous. If, for example, in anterior poliomyelitis, though the central cell is destroyed, there is some tendency toward restoration on the part of the Schwann cells of the fiber itself, there will be at least, a preparedness of the fiber, if subsequently given an opportunity, to make functional connections with other cells.

It must be confessed that the unequivocal acceptation of these views of peripheral autogenetic regeneration has received something of a check through the more recent publications of Langley and Anderson,[15] who have indicated some of the possibilities of error, particularly in Bethe's investigations. Again, the recent discoveries made by Dr. Harrison[16] can hardly be brought into harmony with Bethe's views. This investigator has shown that, if, in a frog embryo, the ganglionic crest, destined to give rise not only to the dorsal root ganglia but also to the cells of Schwann, be removed, naked motor axis-cylinder processes will grow from the remaining intact ventral portion of the rudimentary cord, and make their normal functionating connections with the muscle plates. Further, in studying the outgrowth of the fibers from the cells he has observed that there is a definite wandering or amœboid property of the axis-cylinder process—a discovery which, if correct, completely disproves the postulate of Hensen, that there is some original connection with the periphery which serves during growth to draw the nerve out to its ultimate terminus. Harrison's observations, on the other hand, would indicate the existence of an active outgrowth, influenced by some chemical affinity for its field of destination. In some such way it would seem, the central ends of divided fibers of the adult actively tend to regain their peripheral connections and succeed in doing so unless there be some mechanical interference in the tissue to prevent this. Whether or not there is an autogenetic process of repair in the isolated end of the fiber, or whether the central cell plays the entire part, or, what is not improbable, whether both factors are together concerned,[17] must for our purposes be looked upon as a secondary consideration; it is this normal active chemotactic tendency to unite which chiefly concerns us. In their laboratory experiences, investigators into the problems connected with autogenetic regeneration, have found that the greatest difficulty arises from the fact that it is almost impossible to prevent some reunion of the divided nerve fibers, with their original central ends, or with the central ends of fibers from other sources, which have been unavoidably cut through during the operation. This fact is worthy of mention, because we have long been taught that such a reunion is not to be expected, unless the fibers of a severed trunk are encouraged to find their proper connection by a surgical approximation of the stumps with suture or other means. It seems probable on the other hand, that, unless there has been some gross error in technique—as from the accidental interposition of some other tissue, or a loss or necessary extirpation of a large portion of a nerve, the ends will reunite of their own accord. In the case of the smaller, peripheral nerves, divided during an approach toward deeper parts, we know this to be the usual result, and the more dry and skillful and careful the dissection, and the more painstaking and accurate the apposition of the parts during the closure of the wound, the more complete and rapid will be these reunions. Perhaps these changes can be best appreciated by making a careful study of the post-operative areas of cutaneous anæsthesia and motor palsies after extensive dissections such, for example, as are necessitated during a complete excision of the glands of the neck. In these cases an examination will show that, when the wound has been carefully closed, the anterior cutaneous branches of the cervical plexus and the spinal accessory, which are almost always injured, invariably reunite, even when no attempt has been made to suture them, whereas after a rough operation and a hurried and careless closure of the wound, they will not. The same thing is true after operations over the parotid region in which the N. facialis is so liable to injury. We have always been taught that incisions in this region should be made parallel to the facial fibers, but the text-books in general contain no such warning in regard to operations elsewhere on the body (except in regard to the musculospiral, external popliteal nerve and a few others), because the resultant disturbance, whether motor or sensory or both, being unobtrusive and unlooked for, escapes observation. But to take these points into account even in the case of the smaller and less significant nerves should not be regarded as finicky surgery. Avoidance of injury to nerves, large or small, must always be a desideratum in operations. Here, however, I would only emphasize the fact that after such divisions as are often unavoidable, a careful approximation of the tissues, the avoidance of blood clots and points of necrosis—the organization of which increases the density of the resulting cicatrix—will serve to bring the severed ends of the nerves sufficiently near together, so that the chemotactic influence, whatever it may be, will suffice to bring about reunion. The same is true of the larger nerve trunks, and I doubt not that the suture material used in apposing the stumps of divided nerves,

[15] Autogenetic Regeneration in the Nerves of the Limbs. Journal of Physiology, 1904, Vol. 31, p. 418.

[16] Neue Versuche und Beobachtungen über die Entwicklung der peripheren Nerven der Wirbeltiere. Bonn, 1904.

[17] It does not seem at all improbable that it may be some chemical affinity, exerted by the proliferating cells of Schwann at the periphery upon the amœboid-like downgrowth of the axis-cylinder processes, that leads them to their proper destination. Both factors may, on such an explanation, be actively influential in the regenerative process and not one of them alone.

by increasing scar-formation, frequently serves to defeat the very ends for which it has been employed.

Langley in the course of his investigations was the first, or among the first, to put to experimental test the possibility of nerve crossing, through which has been opened up such a promising field for peripheral nerve operations. During the process of reunion of a divided nerve it is hardly conceivable that each fiber will make connection with its own original fiber in the peripheral stump and thus find its way to its original end organ. If this is so, why should it not be possible to graft the peripheral end of one severed nerve, whose central connections have been destroyed, with the central end of another nerve of like nature, which has not suffered injury? It has been shown that not only is this possible, but that, at least for the extremities, a reeducation of the central activities takes place, particularly in young individuals, to such a degree that practically the normal function is resumed, one group of cells sufficing to preside over its own, as well as over the territory of the nerve originally injured, proving itself capable, as it were, of driving a team as well as a single horse. More simple even than in the case of mixed nerves would seem to be possibilities of anastomosis between two purely somatic efferent nerves, and the idea of grafting a neighboring intact motor nerve into a paralyzed facial branch, in the hope of overcoming the seriously obtrusive deformity, occurred a few years ago almost simultaneously, to surgeons in England, France, Germany and this country, and was acted upon with results which doubtless are known to you.[18]

In three of my own cases I decided upon the spino-facial form of anastomosis; and though the hypoglossal, from what would appear to be merely conjectural reasons, is favored by others, the functional results after the latter operation seem in no instance to have been comparable with those after the spino-facial grafts. But no matter by what method they may be performed, anything short of an absolutely perfect result in these cases will show itself plainly by some asymmetry during the finer expressional movements. This would not be the case after anastomoses between the limb nerves and it is here, in dealing with the paralyses of anterior poliomyelitis, that we may expect to find the field of greatest promise for the application of these principles. Let us take a simple illustration. Terminal paralyses or palsies of certain groups of muscles characterize the residual features of an anterior poliomyelitis. The destruction of the ventral-horn cells is most intense in certain spinal segments;[19] the cells of the adjoining ones, having suffered less severely, ultimately resume their normal activity and so, up to a certain point, the early wide-spread paralyses disappear. Thus, let us suppose that the ventral-horn cells, which give rise to the fibers of the peroneal nerve and which are clustered largely (?) in the first sacral segment, have been for the most part destroyed. A paralysis of the peronei and of the extensors (dorsal flexors) of the toes and ankle results, leaving the foot and ankle unbalanced and often useless, owing to the lack of opposition to the pull of the sound flexors and supinators. If done at the proper time, an intentional section of the degenerated peroneal nerve and an implantation of its peripheral stump into an incision made into the functionally intact internal popliteal, should restore the balance as no tendon transplantation could possibly do; for, unless there is some flaw in the entire argument, the divided central ends of the internal popliteal fibers should, without discriminating between them, grow down and make connections with the originally degenerated fibers of the peroneal and also with the newly degenerated ones that lead to the nerve's natural field of peripheral distribution. Many of these operations have already been done and it remains only to determine the time most advantageous for the anastomosis. It is probable that after it has become evident what the extent and what the seat of the residual palsy are likely to be, the earlier the operation is carried out the greater will be the probability of success. Possibly just when the peripheral changes in the degenerated nerve, supposed to be reparative in nature, are at their most active stage, may be the most desirable time. Certainly after these changes—whatever be their nature—have retrogressed and the muscle spindles and end-organs have atrophied, the chances for restoration of control are much diminished.

More complex problems arise when the paralyses are diffuse and scattered; as, for example, when the movements at the knee and hip are affected or the upper arm is palsied. On one child from Dr. Thomas' clinic, that presented this extreme type of paralysis with an involvement of all four extremities, I have done several operations. In the upper part of the cord the fifth cervical segment was particularly the seat of injury, the deltoids being absolutely, and the biceps and supinator muscles in large measure paralyzed. The spinal accessory has been sacrificed and transplanted into the upper radicle of the brachial plexus. Anastomoses have likewise been made on each of the lower extremities. On the side most seriously crippled, the N. femoralis being the only nerve that had remained in large part intact, it was anastomosed in the pelvic fossa with the obturator and first radicle of the sacral plexus with the hope of restoring power, in the thigh, sufficient to let the child stand and possibly walk. Of course, in cases of this kind, no tendon transplantation could be of service.

It is quite possible that there are other maladies which may be greatly benefited by measures conducted along these same lines. Kennedy, it will be remembered, cured a patient, who was suffering from an extremely trying facial (motor) tic, by deliberate division of the N. facialis and an immediate spino-facial anastomosis. I have recently had a similar case. After reading some of Bethe's experiments, I have vainly looked for a proper case in which to anastomose central end to central end

[18] The bibliography of the subject will be found in Ballance and Stewart's article in the London Lancet, May, 1902; and at the end of the writer's paper in the Annals of Surgery of the same date.

[19] Segmental in much the same way as is the best known of the diseases of the dorsal-root ganglion cells (herpes zoster) for which Head has suggested the name posterior poliomyelitis. The toxic agent, whatever it may be, in each disease has an especial affinity for one or the other variety of these cells. There is usually a rapidly acquired immunity which spares the remaining cells, and which usually persists for life.

of the nerves of an amputation stump, when there existed an intractable neuralgia originating in the so-called amputation neuromata. Unions of this nature, the "polarity" of the opposed ends being the same, are of course, unaccompanied by any functional transmissibility in the nerve, but they probably would suffice to prevent the formation of the terminal and painful tangle of outgrowing axones.

The possibilities of nerve anastomosis do not end here with the grafting of like upon like, for Langley has demonstrated the surprising fact that nerves, normally subserving a different function, may, under favorable circumstances, be interposed. Thus he and Anderson[20] found that certain somatic efferent nerve fibers, such as are contained in the fifth cervical nerve, are capable of making a functional union with the preganglionic fibers of the cervical sympathetic, and vice versa. For example, the preganglionic fibers of the sympathetic may unite with the peripheral ends of the recurrent laryngeal, phrenic, or spinal acessory. It is quite within the realm of probabilities that this principle may be applied to a great number of neurological conditions, to cases of bulbar palsy for example, or to restore tone in the muscles of a paralyzed larynx, however it may have been produced.

With these crude generalizations I must close this section of my paper on the peripheral nerves, leaving much unsaid of the particular operations such as those for torticollis, for paralyzing lesions of the brachial plexus—whether from injuries at birth or in adult life, of neurectomy for Bernhardt's paresthetic meralgia, of the operations for tetanus suggested by the discoveries of Meyer and Ransome,[21] of cervical sympathectomy for glaucoma and exophthalmos, and, indeed of the entire surgery of the sympathetic, a large subject of itself. The particular disorders of many individual nerves—the trigeminus, for example, in its relation to congenital nævi, herpes, morphœa, neuralgia and other phenomena of disease—would alone be enough to write a book upon.

And now that all has been said, which may justly be crowded upon the pages of a single address, may I, for a moment, in closing, return again to my introductory theme? In talking the matter over with my surgical friends, many of them have expressed themselves emphatically against any form of operative specialization. But, granting the wisdom and necessity of a general surgical training beforehand, I do not see how such particularization of work can be avoided, if we wish more surely and progressively to advance our manipulative therapy. Are practice of hand and concentration of thought to go for nothing? Whether as the result of individual fitness, or opportunity, or training, certain things must be better understood, and, from purely a handicraftman's point of view, better done by one man than by another. Gowers has said that "the separation of medicine from surgery is itself specialization."[22] In this sense everyone specializes, and the misfortune to medicine of its long divorcement from surgery, its only inductive branch, has been recently emphasized by Clifford Allbutt. We all are, or should be primarily internists, but although all build on the same foundation, some by inclination or fitness prefer the mechanical side of therapy. The same principle applies to the sub-departments of medicine, and in this particular field of neurology some of those who finally focus their studies in this direction, must, in aid of their scant therapeutic resources, do their own operating.

What Billroth, in the early days of abdominal surgery, said of the future of medicine in general, is just as applicable to this smaller field: "Die innere Medizin müsse mehr chirurgisch werden."

[20] Langley and Anderson, The Union of Different Kinds of Nerve Fibers. Journal of Physiology, 1904, Vol. 31, p. 365. This, their more recent publication, contains a summary of the earlier work which has appeared under various titles.

[21] Archiv f. Exper. Pathol. u. Pharm., 1903, Vol. XLIX. They have shown that the neurones are protected with remarkable efficiency against circulating tetanus toxin, and that the central cells are reached only by way of the long paths of their axis-cylinder processes, which must first suffer injury before the poison can effectually enter them. The long incubation period is taken up with this slow process of attack through the muscle "Endorganen." The toxin travels cellulipetally after entering the nerve fiber and thus it is possible by an early exposure of the nerves, central to the point of lesion, and by the local (intra-neural) injection of antitetanotoxin to effectively combat the progress of the intoxication.

[22] I wish to quote, in this connection, a paragraph of some historical interest from John Morgan's "Discourse upon the Institution of Medical Schools in America," Phila., 1765.

"First, I propose to confine myself, in practice, to those cases which belong most immediately to the office of a Physician, that I may prescribe for and attend such cases to greater advantage. I shall therefore avoid, all I can, interfering in the proper business of surgery, viz., manual operation."

TUMOR OF THE PARATHYROID GLAND.

By W. G. MacCallum, M. D.,

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Two tumors arising from the parathyroid gland have been described, the first by Benjamins[1] and the second by Erdheim.[2] In Benjamins' case a tumor the size of a child's head developed rapidly in the thyroid region and was extirpated. It was surrounded by a capsule in which at one point a normal parathyroid was found. Its substance was made up of broad strands and masses of epithelial cells resembling those of the normal parathyroid, with very slightly tinged protoplasm and vesicular nucleus. Toward the connective-tissue stroma there was almost everywhere a palisade row of cells taller and with

[1] Benjamins, Zieglers Beitrage, Bd. 31, 1902, p. 143.

[2] Erdheim, ibid., Bd. 33, 1903, p. 158.

deeper staining nucleus than the rest. Occasional colloid droplets were seen.

Erdheim describes a nodule 2¼ x 1½ cm. in size, found at an autopsy in an 18-year-old person, at the lower pole of the thyroid, without being more directly connected with that organ. No other parathyroid glands could be found. Microscopically this tumor consisted of strands and irregular masses of cells with relatively sparse vascular supply in the delicate stroma. The cells corresponded with those of the normal gland, even the oxyphile cell groups being found. Colloid droplets were observed between the cells although there were no definite follicles. In one section a cyst was found, lined with one layer of cells and containing degenerated fatty cells. Erdheim suggests the possibility that since the other parathyroid glands were not to be found this may have begun as the result of a work hypertrophy, which gave the impulse to tumor formation.

At an autopsy in the case of a young man æt. 26, who had suffered for several years from symptoms of a chronic nephritis and on whom two years ago the operation of decapsulation of the kidney had been performed in the Johns Hopkins Hospital, there was found on the right side just below the lower pole of the thyroid and quite separate from it a round smooth mass enclosed in a delicate capsule and lying in the loose connective tissue. This mass measured about 2 cm. in diameter was almost spherical, being somewhat flattened. Externally and on section it was of a uniform opaque whitish-yellow color and in consistence was rather soft. On section the cut surface of the homogeneous slightly granular substance of the mass bulged outward. In the center was a small cavity with smooth walls containing a clear fluid. The mass was not richly supplied with blood-vessels.

Two well formed parathyroid glands were found which both macroscopically and microscopically were normal. The thyroid was normal throughout. Otherwise the chief lesion to be noted was an advanced chronic diffuse nephritis. The patient died in uræmia.

The mass was fixed in Zenker's fluid. Microscopically it proved to be composed of a tissue which, as in the cases of Benjamins and Erdheim, most closely resembles that of the parathyroid. There are strands and very large anastomosing branched masses of cells which are separated by a relatively delicate stroma which bears the blood-vessels. Compared with the normal parathyroid, the blood supply is extremely meager. The columns of cells are usually solid, the cells being packed together and pressing one another into polygonal forms. Sometimes there are as many as 24 cells abreast in such columns, but most of the strands are not so bulky and may be so small as to contain only two or three cells abreast. Some of the larger solid-looking masses are found to be permeated by a network of filaments of the stroma, bearing blood-vessels. The cells are quite as they are in the normal parathyroid showing vesicular nuclei and protoplasm which may be faintly granular or perfectly clear and free from any stainable granules. Solid masses of these latter cells occur and there is one especially large wedge-shaped area composed of them alone. Large and small groups of cells corresponding precisely with the normal oxyphilic cells of the parathyroid are scattered here and there among the other cells. Their protoplasm has the appearance of ground glass and takes a deep eosin stain. Their nuclei vary somewhat in size, but stain more deeply than those of the other cells. Mitotic figures of great beauty occur in all these cell forms.

The palisade arrangement of the peripheral cells is not especially striking in the great mass of this tissue, nor does it seem so to me in the normal parathyroid. There are certain of the masses of cells, however, in which a central cavity is found about which the cells are often arranged as a palisade. This is less marked when the cavity is surrounded by many rows of cells than when its wall is formed, as it frequently is, of a single row in which the cells then become high and columnar with the nucleus peripherally placed. These cells sometimes appear to possess cilia, but of that I cannot be sure as they are very imperfect. Not only the ordinary cells but the very clear variety and the oxyphilic cells may take part in forming the walls of these follicle-like cavities. The cavities are sometimes rounded and small, sometimes quite large and elongated or branched. They contain sometimes a finely granular coagulum, as if a thin watery albuminous fluid had been coagulated there by the fixing fluid. Oftener they are filled with bubble-like vesicles of about the size of red corpuscles and somewhat resembling shadows of those cells. The variation in their size, however, makes it seem that they are really analogous to those vesicle-like structures, so frequently seen in the renal tubules. Desquamated epithelial cells also occur there and occasionally red corpuscles. In one or two alveoli there are masses of red corpuscles, some well preserved, some broken down, together with particles of blood pigment, indicating that a hæmorrhage had occurred some time before death.

Of colloid-like material there is practically no trace either among the cells or in the alveolar spaces.

The larger cavity which was opened in cutting through the mass is found to be lined with one layer of flattened epithelial cells, which have been in large part desquamated. It contains a fluid a little of which has adhered to the lining wall and is coagulated into a finely granular almost colloid-like pink staining material.

The capsule is delicate and consists of fibrous tissue into which the epithelial cells do not extend.

It is evident that except in bulk, in the size of the cell masses and in the formation of such definite cavities this growth differs in no way from the normal parathyroid unless it be in that there is no adipose tissue between the cell strands. The question therefore arises as it did in Erdheim's case as to whether we should regard it as a tumor or as the result of a compensatory hypertrophy. Erdheim was moved to the suggestion of the possibility of a vicarious hypertrophy by the absence of the other parathyroid glands. In this case, however, two other normal parathyroids were present. On reviewing the anatomical conditions elsewhere in the body, the only

other suggestion that arises is the possibility that in the state of extreme renal insufficiency, which had existed for so long, extra demands might have been made upon the parathyroid.

Two other cases of advanced chronic nephritis in young persons were studied and in the parathyroids in one abundant mitoses were found, while none were to be seen in the parathyroids of the other.

No evidence of invasive growth is to be found, and in the absence of any convincing explanation for a compensatory hypertrophy it seems that we shall have to speak of this as an adenomatous new growth, while recognising the fact that many so-called adenomata in glandular organs have turned out to be evidences of compensatory or regenerative hyperplasia.

BACILLUS VIOLACEUS MANILÆ.

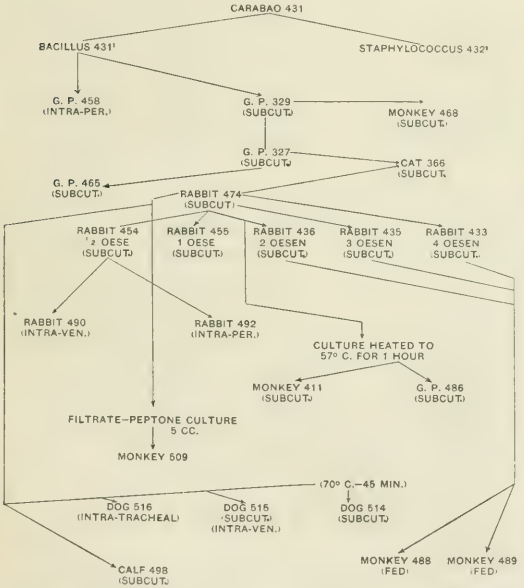
(A PATHOGENIC MICRO-ORGANISM.)

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I can find no account, in literature, of a pathogenic organism similar to the one of which a description follows, but there are one or two bacilli, which resemble it so closely in morphologic and cultural characteristics, that it seems wisest to consider the present germ as simply a variety of certain well-known but, at least usually, non-pathogenic forms.



A Scheme to Show the Course of the Inoculation Experiments.

The group, to which reference is made, is the one the individual members of which are discussed collectively by Migula (System der Bakterien, 1900, II, 939), under the title of *Pseudomonas violacea*, and which are separately described by other authors as *B. violaceus, B. violaceus Berolinensis, B. violaceus Lutetiensis, B. violaceus Laurentius*, etc.

The organisms are described by these authors as bacilli, which are short or of medium length, sometimes somewhat bent, and with rounded ends. The measurements are about 1 x 0.65 μ, although some individuals may attain a length of 3 μ. In cultures on agar and potato, formations much resembling spores, but which are like these reproductive bodies in appearance only, are seen within the individual rods. These pseudo spores are considered to be either plasma globules, or vacuoles, and true spores have not been demonstrated. The rods are motile; sometimes, as in cultures kept at body temperature, quite actively so. They possess a single polar flagellum. Deep colonies in gelatine have an irregular rounded appearance, with projecting filaments. On the surface the colonies form small depressions, in which blue-gray masses of bacilli are seen. The color gradually becomes more intense, and the straggling filaments grow out into the surrounding medium. On agar the growth is blackish-violet. Blood serum is liquefied—peptonized. On potato the growth spreads over the surface of the medium, and forms a rich pigment, which does not stain the whole fragment of the vegetable, but only that portion immediately beneath the growth. Broth is clouded, and a dirty white sediment falls to the bottom of the tube, and takes on a pale violet color. No pellicle is formed on the surface. The organisms grow fast at room temperature, but more slowly than most water bacteria, and they do not grow beneath the isinglass. They are most readily stained with hot carbol-fuchsin, and are decolorized by Gram's method.

B. Violaceus Manilæ corresponds with the above descriptions in some details, but in some it does not. This organism is a short rod, measuring approximately 0.5 x 1.0 to 1.5μ. Occasional rods are even longer. It stains with the usual aniline dyes, best perhaps with carbol-thionin, or with carbol-fuchsin or gentian-violet diluted five times with water. It is not stained by Gram's method, and is not "acid-fast." When well stained by any of the above mentioned solutions, it appears as a short, thin bacillus, very frequently slightly bent, and with rounded ends. It does not, as a rule, stain uniformly, and may show one or more clear spaces which are not tinted, and which appear remarkably like spores. These clear spaces cannot be stained by the usual methods used in

coloring spores. The organisms are generally single, sometimes in pairs, occasionally arranged in short chains of 3 or 4 individuals. They are motile, usually sluggishly turning and twisting, but frequently single rods may be seen to cross the field of the microscope with a more rapid, wriggling motion. Each organism possesses one polar flagellum. In rare instances two flagella may be distinguished springing from the same pole of the bacillus.

On agar plates, within 24 hours at 37 degrees C., colonies appear as small, round, violet-gray spots. These slowly enlarge and become deeper in color. The maximum depth of color is attained in from 48 to 72 hours. As the colonies grow, their margins become slightly irregular, and with a rather indefinite concentric arrangement of layers, which are somewhat thicker towards their peripheries, with the result that the centers of the colonies have a less intense blue color than the edges. These masses of organisms are slightly tenacious, but after removal from the medium are readily dissociated in water. The growth on agar slants is similar to that on plates; extension being slow, but rather even, resulting in a very slight crenation. The water of condensation is clouded and bluish, with a blue sediment. In stab-cultures in agar the growth is scant, and no pigment is formed below the surface.

Gelatine is liquefied slowly at the temperature of the ice-box, the growth forming a funnel-shaped area with a cup-shaped upper portion. The sediment is bluish.

Bouillon is diffusely clouded. A delicate pellicle is formed, which, upon 1 per cent alkaline material, is but slightly pigmented, but which is better developed and bluer on a 1 per cent acid liquid. The sediment in 1 per cent acid bouillon is pale violet-blue, and rather viscid.

Dunham's peptone solution is also clouded, and a thin pigmented pellicle is produced. A sediment is deposited in this medium, which resembles that in broth, but in which more pigment is present. The whole medium becomes diffusely bluish within 48 hours.

On potato the growth extends over the whole surface of the medium, and to the water of condensation. The pigment production is luxuriant. The superficial layers of all the solid medium are stained by the soluble blue pigment. In sugar-containing media—glucose and lactose—no gas is formed.

The reaction of milk, after seven days, is slightly acid, but there is no coagulation. However, the casein is peptonized, and the upper third of the tube becomes almost clear, being faintly violet.

The organism thrives better and produces pigment somewhat more freely at 37 degrees C., than at lower temperatures; it does not grow at all well, and does not produce any pigment, below the surface of a solid medium. It is almost an obligatory aërob. It is killed by boiling for one minute; by a temperature of 67 degrees C., after an exposure of 5 minutes; and by a temperature of 57 degrees C. after one hour. It does not form spores.

The pigment is soluble in alcohol, giving a deep, rich, violet solution. It is slightly soluble in water, barely dissolved in ether, and insoluble in chloroform.

The organism described above has been isolated from three carabaos, which died suddenly with such noticeable absence of clinical symptoms, that acute hemorrhagic septicæmia was suspected. In two of these cases, Dr. Jobling obtained cultures of this organism from the lymph-glands and lungs, and in the third case the writer found it predominating in cultures from the same organs. Later on, in the press of work, the cultures from the first cases were lost, and only those from the third were used in the following investigation. However, Dr. Jobling had injected his organisms into guinea-pigs, producing the same kind of lesions which I shall describe. The details of the first autopsies are meager. Little can be said, except that the prescapular glands resembled those to be described in connection with the third case.

Like the first ones, the third animal died suddenly. It had had no rise in temperature, as far as the records of the corral show, and symptoms of rinderpest were absent. On removing the hide, none of the gross lesions of hemorrhagic septicæmia or surra were encountered—neither hemorrhages nor œdemas. The prescapular glands were enlarged and intensely injected, but neither showed true hemorrhages nor necrotic areas. There were a few small petechiæ under the visceral pericardium, and under the endocardium of the left ventricle. The lungs were not collapsed, but were for the most part crepitant. The surfaces of these organs were dotted with small pale areas varying in size from that of a pinhead to a small hazel-nut. These areas were firm and projected slightly above the surface of the pleura. They were not round, but irregularly stellate, and each was surrounded by an appreciable zone of congestion. On section they appeared granular and gray, and with no indication of caseation or suppuration. Other non-crepitant areas, which occurred chiefly along the anterior margins of the lungs, had much the appearance of red infarcts. They were dark red, and raised above the general surface of the organ in which they occurred. On section they were dark and moist, simulating the stage of red hepatization in pneumonia. The lungs on section were generally pale and œdematous, and in their substance contained large numbers of the small miliary nodules, similar to those seen upon their surface. The spleen appeared to be normal. The liver showed no macroscopic changes. The gall-bladder was somewhat larger than normal, but the stomach showed no pathologic lesions visible to the naked eye, nor were any found in the trachea, pharynx or tonsils. The kidneys were perhaps a trifle pale. The intestinal tract was normal.

Smears from the prescapular glands showed a few very small organisms, which appeared as diplococci or polar-stained bacilli, and a large number of somewhat larger rods; some of these irregularly stained, and others curved. Cover-glass preparations, made from the nodules of the lungs, showed almost nothing but small bacilli, which stained unevenly. Smears from the heart showed no organisms.

Cultures from the blood gave no growth after some days, and those from the lung lesions produced a few colonies of

a large thick bacillus, resembling B. subtilis, and other colonies in very much larger numbers, (in one plate, these latter only), which developed a blue color after 24 hours at 37 degrees C., and which were composed of the organisms which have been described. In cultures from the prescapular glands two organisms were demonstrated. One was identical with the chromogenic one isolated from the lungs, the other was a small coccus arranged mostly in clumps, which, after several days, produced a very faint yellow color. Both of these organisms, the coccus and the chromogenic bacillus, were studied carefully. One was in all probability a modified staphylococcus aureus, which produced a minimum of pigment, coagulated milk very slowly with coincident reduction of the litmus, and which did not kill guinea-pigs in reasonable doses, either when injected into the peritoneal cavity, or under the skin. The other has been described in its cultured and morphological character, and corresponds quite closely with Bacillus violaceus (Schröter), or Pseudomonas violacea (Migula). In none of the books, to which we have access, have I been able to find any reference to the pathogenicity of Bacillus violaceus. This makes the following experimental study of some interest:

One cubic centimeter of a 48-hour-old culture from the lung of the carabao (No. 431), was injected under the skin of a guinea-pig (No. 329). The animal became quite ill within the next 24 hours, and a large semi-fluctuating mass appeared at the site of the inoculation. Coincidently, the temperature, which previously had been running between 36.5 degrees and 38.4 degrees C., rose to 39.8 degrees C., and then dropped gradually until the animal died. Death occurred on the fifth day after infection.

At autopsy a large area of necrosis was found under the skin about the point of inoculation. This was surrounded by tissue in a state of coagulation necrosis, in which were occasional lacunæ filled with a dark gelatinous material. There was no true pus, and no hemorrhages appeared, although the adjacent tissues showed extensive congestion. The peritoneal cavity contained a small amount of a clear fluid. The lungs were the seat of large and small hemorrhagic infarcts, the lower lobes of both sides being almost completely infarcted. The spleen was markedly enlarged, was very dark, soft and mottled with miliary gray spots, resembling focal necroses. The liver was also thickly studded with similar areas. There were no macroscopic lesions in the heart or kidneys, though the latter were pale. The adrenals were markedly enlarged, their medullæ congested and with small areas of necrosis in the cortices. The lymph glands of the axillæ and groins were enlarged and injected. Nothing abnormal was remarked in the intestines, stomach or bladder.

Smears were made from the subcutaneous tissues at the site of the primary lesions, from the lungs, spleen, liver, lymph glands and heart. All save those from the heart showed numbers of rods morphologically identical with those which had been injected. the organism was recovered in pure cultures from the liver, peritoneal cavity, lungs, the primary lesions and the heart.

A second guinea-pig (No. 458), was inoculated intraperitoneally with one-half of a cubic centimeter of a bouillon culture obtained from the carabao. It survived the operation.

From the cultures obtained from the first guinea-pig, a second (No. 327), was inoculated with ½ cc. of an emulsion made with three loopfuls of a 24-hour-old agar culture in 5 cc. of a normal salt solution. The animal died on the third day after inoculation. The anatomical picture was the same as that in the first guinea-pig, except that in the lungs small miliary necroses were present in place of the infarcts noticed before. Pure cultures of the experimental organisms were obtained from the heart, liver and the subcutaneous lesions.

With 1 cc. of an emulsion, made with 3 loopfuls of the organisms, obtained from this last animal, and 5 cc. of salt solution, a rabbit (No. 474) was inoculated subdermally. It died within 36 hours. Autopsy showed a bloody fluid in the peritoneal cavity, a wide-spread hemorrhagic lesion at the site of inoculation with no suppuration, but with necroses in the liver. The organisms were recovered in pure culture from the peritoneal cavity, liver and heart. At the same time, a guinea-pig inoculated with an equal amount of the same material, died within 20 hours. The only macroscopic lesions were miliary abscesses of the liver. Cultures were obtained from the heart, liver and peritoneal cavity.

A cat (No. 366), was inoculated under the skin of the belly with 1 cc. of an agar suspension of a culture obtained from guinea-pig No. 327. The succeeding day a large semi-fluctuant mass surrounded the point of inoculation. The second day after infection, this abscess was discharging externally by a sinus, the edges of which were ragged, and about which the skin was semi-necrotic. Eventually, all the skin about this first sinus sloughed, leaving an ulcer measuring 5 x 5 cm., whose base was on the subjacent muscles, and whose edges were regular, indurated and undermined. This ulcer gradually healed, and the animal showed a complete skin on the 30th day after inoculation. When recovery had been established, a second dose of a suspension of the organism from No. 474 was introduced hypodermically. No lesion was produced. The serum from this animal taken at this time agglutinated the specific organisms in a dilution of 1-60 after about 40 minutes; in dilution of 1-200, after about 1 hour and 15 minutes.

Five rabbits were inoculated with different amounts of the organisms to show what variations occurred in the lesions, if possible. The first (No. 454), received ½ a loopful, the second (No. 455), one, the third (No. 436), two, the fourth (No. 435), three, and the fifth (No. 433), four, of a culture obtained from rabbit No. 474. All of these animals died; Nos. 454, 455 and 436 in three days, No. 435 in four days and No. 433 in five days after inoculation. From all, the organism was recovered from the tissues and heart's blood, except in two cases (No. 435 and 436), in which the cultures from the heart were negative.

The progressive changes in the organs of these animals was noticeable and interesting. In animal No. 454 the subcutaneous jelly-like œdema was present; there were miliary ab-

scesses in the liver, none in the spleen, none in the lungs, which were simply injected. In animal No. 455 there were a few nodules in the lungs and in the liver; the other organs appeared like those in animal No. 454. In animal No. 436 there were large abscesses in the lungs, and but a few small ones in the liver. Animal No. 435 showed similar lesions. In No. 433 there were a few very small abscesses in the liver and spleen, while the lungs were generally consolidated, showing comparatively large areas composed of collections of miliary abscesses. In other words, the lesions varied as the dose of the organisms, and while with small doses the liver was more prone to be affected, with large ones the lungs were more prominently diseased. This may, or may not, be true for other animal species. At any rate, the principal feature of the pathogenic action of the bacillus is its necrotizing power.

A dog (No. 515) was inoculated subcutaneously with 1 cc. of an agar suspension of a culture from No. 474. Several days later a local lesion appeared, which resembled that produced in the cat, but which was less extensive and healed more rapidly. About three weeks afterwards, this dog received 1 cc. of similar material in the femoral vein. Following this injection the animal was irritable, eating but little for a few days. On the third day, and continuing for four days, tremors were noticed in the head and limbs, the animal lying quietly without seeming to suffer. He subsequently became entirely well.

In the case of another dog (No. 516), in which the organisms were introduced into the trachea, no illness followed.

A calf was inoculated in the dew-lap with 2 cc. of the same material which was used with the dogs. The day following inoculation there was a large, painful œdematous mass visible in the region of infection. This enlarged until it reached the size of a large fist, and then gradually disappeared.

Inoculation into the peritoneal cavity of 1 cc. of a 48-hour-old agar culture suspended in salt solution, caused the death of a rabbit (No. 492), within 12 hours. At autopsy there was nothing to be seen, except evidence of an acute peritonitis. Cultures from heart and peritoneal cavity were positive and pure.

Intravenous inoculation of $\frac{1}{3}$ cc. of a 48-hour-old agar suspension killed a rabbit (No. 490), within 10 hours. No lesions were visible to the naked eye. Cultures made from the heart, peritoneal cavity, and pleura showed the organisms in uncontaminated growths.

Feeding experiments were negative. Large quantities of virulent agar cultures were fed to two monkeys (No. 488 and 489) with no ill effects.

Experiments upon serum reactions were begun with a monkey (No. 468), which had received a dose of one cubic centimeter of an emulsion made from a 24-hour-old agar culture of the organisms isolated from the carabao. The monkey did not succumb to this first subcutaneous injection, and four days later a second one was made with $1\frac{1}{2}$ cc. of an emulsion made with a 24-hour-old culture of the organisms isolated from the second guinea-pig (No. 327). The day following this second injection, a small quantity of blood was withdrawn and its agglutinative powers tested. In dilutions of 1-20 a complete agglutination was present at the end of 15 minutes. In 1-40, a complete reaction was given in half an hour. In a dilution of 1-200, the result was positive and complete in one hour.

Later this animal was inoculated subcutaneously with $1\frac{1}{2}$ cc. of an agar suspension made with a culture of the organisms recovered from animal No. 474. Two days afterwards a large slough appeared on the abdomen about the point of inoculation, and the animal was very ill. It was killed and the blood drained off into a sterile tube. The serum obtained from this blood was tested for its agglutinative and bactericidal powers. In a dilution of 1-200 agglutination was complete in 20 minutes; 1-400 in 30 minutes; 1-600 in 45 minutes; 1-1000 in 50 minutes; 1-2000 incomplete after 1 hour; 1-4000 was negative.

This experiment was repeated in small tubes, so that the reaction could be watched with the naked eye. The tubes were allowed to stand over night. The next day all the organisms were contained in a precipitate, except in the control tube, in which the liquid was still cloudy. Cultures made from all these tubes gave luxuriant growths. No appreciable bactericidal action was present.

To determine whether or not a soluble toxin was produced, a four-day-old culture in peptone was filtered through a Pasteur-Chamberland bougie F. The filtrate was kept at 37 degrees C. over night and no growth occurred. The next day 5 cc. of the material was injected under the skin of a monkey (No. 509). Following this there was no sign of toxæmia, no rise of temperature, nor any sign of altered health in the animal.

After it had been proved that even very small amounts of the living organisms would cause death of small animals, and at the same time produce the specific lesions without the appearance of any appreciable immunity, cultures were heated to 57 degrees C. for one hour and these dead cultures, suspended in normal salt solution, were used for injection.

This material was used subcutaneously in a guinea-pig (No. 486), and a monkey (No. 411). In the case of the monkey, 1 cc. of an agar suspension was used for the first injection. There was no appearance of a reaction until the fifth day, when the temperature rose one degree above the normal one for the animal. The day following this reaction, a second injection of the same amount of the same material was given. On the fourth day following, the blood was tested for its agglutinating powers. Complete agglutination was accomplished in dilutions of 1-400 in 15 minutes. A third inoculation was then made with 0.75 cc. (intraperitoneal) and 0.75 cc. (subcutaneous), of the same material which had been used for the other inoculations, and four days later a fourth inoculation was made with $2\frac{1}{2}$ cc. subcutaneously. Two days after the last inoculation, the monkey was found dead. At autopsy there were no macroscopic lesions at the site of the last inoculation, where there was a small pocket of a bluish material. Cultures from this lesion, from the heart, liver and spleen were entirely negative, and the media was perfectly

sterile after five days. The serum taken from the heart at autopsy gave a perfect agglutination in a dilution of 1-1000 in 40 minutes. The guinea-pig suffered no harm from the inoculations.

Later, using cultures of the organisms from animal No. 474, and which had been killed by heating to 70 degrees C., for 46 minutes, a dog was inoculated with a series of injections. He remained well throughout the time. However, after the third inoculation his blood agglutinated in a dilution of 1-20 only, after one hour.

The essential lesions produced in experimental animals are found at the site of inoculation, in the lungs, liver, lymph glands and spleen.

At the site of inoculation, when infection has been caused subcutaneously, there is a wide area of necrosis with local and circumambient œdema resembling the lesions produced by the diphtheria bacillus. The whole area may undergo necrosis, become gangrenous and slough away.

In the rabbits, the œdema has been more marked than the necrosis. In the cat, the necrosis occurred with but little œdema. The monkeys showed œdema as well as necrotic and gangrenous processes, as did the guinea-pigs.

The lesions in the parenchymatous organs are miliary abscesses, which may show a suppuration stage. In the lungs and liver the surface of these abscesses may be covered with a fibrinous exudate. The bacilli are found in all the lesions.

The losses in stock due to infection with B. violaceus Manilæ, are not extensive, and there seems to be little danger of an epidemic. In all our work we have seen but these three cases. Each was in a different herd, and these herds were widely separated from each other.

So far as treatment is concerned, there is little to be said. All the animals have died so suddenly and unexpectedly, that there was no time either for experiment or speculation on this subject.

A REPORT UPON THE AGGLUTINATION REACTIONS OF THE BACILLUS DYSENTERIÆ (SHIGA) WITH THE BLOOD SERUM OF PATIENTS SUFFERING WITH SUMMER DIARRHŒA.[1]

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The accompanying table (Table I) is the summary of what is by no means intended as an exhaustive study of the problem of the agglutination reactions of *B. dysenteriæ*, but simply of the work done during the summer of 1903, at the Thomas Wilson Sanitarium as a matter of routine upon the blood reactions of the cases of dyspeptic diarrhœa. Unfortunately it does not include all patients treated at the Sanitarium during that time, for in the rush of the clinical work of midsummer many cases were of necessity allowed to pass unexamined.

The report is based upon examinations of the blood of one hundred patients (patients with two admissions with blood examinations on each admission being counted twice), in a few instances upon two or more occasions; of these 45 gave positive (including No. 287), and 55 negative results. No result is reported as positive unless the reaction occurred at a minimal dilution of 1-100, though every case was tried 1-20 and 1-50, and in the table a few such cases are recorded (136, 146, 147, 151, 161). When possible all dilutions were carried up to 1-1000, and in a few cases to 1-1500.

The relation between reaction and clinical diagnosis is seen in Table II, the diagnosis "Dysenteria infantum" being applied, as suggested by Knox, to those cases from whose stools the dysentery bacillus was isolated.

TABLE II.
Blood Examination.

	No. of cases.	Pos.	Neg.
Dysenteria infantum	40	26*	14
Dyspeptic diarrhœa and ileocolitis	42	12	30
Dyspeptic diarrhœa, with malnutrition	4	2	2
Malnutrition and marasmus	11	5	6
Diarrhœa, simple	3	0	3
	100	45*	55

* Includes No. 287.

Thus it will be seen that while 40 cases in a total of 86 cases of dysenteria infantum and dyspeptic diarrhœa gave a positive reaction, 5 cases in 11 cases of malnutrition and marasmus gave such reaction, and of the 3 cases of simple diarrhœa none gave such reaction. Of the forty cases of dysenteria infantum, twenty-five (62.5 per cent) gave a positive reaction and fourteen a negative one; one was not tried through oversight before serum was given on patient's second admission, (287) but it was positive on his first admission (219). This seems a large percentage of negative reactions until one analyzes these cases giving negative results. Four were cases of less than one week's duration (195, 210, 221, 222), one reacted on a later admission 1-1000 (169), one reacted 1-50 (151),

[1] This paper has appeared in abstract in the report of the Rockefeller Institute for Medical Research upon the Diarrhœal Diseases of Infancy.

TABLE I.

Clinical Number.	Clinical diagnosis.	Reaction.	Dilution.	Time of observation.	Day of Disease.	Organism.	Blood in stools.	Mucus in stools.	Number of stools in 24 hours.	Bacteriolog. Diag.	Serum given.	Result.	Remarks.
123	Marasmus. Dysenteria infantum.	+	1–1000	1	3	M[1]	+	+	3–8	+[6]	++[2] +	Died.	Died at home, 3 days after discharge. Fly-borne infection?
132	Dysenteria infantum.	+	1–1000	5	28	H[3]	+	+	6–14	+	+	Died.	
136	Dysenteria infantum. Eclampsia.	+	1–50	3	9	H	+	+	11–16	+	0	Died.	Pus in stools. Blood taken at autopsy.
137	Dysenteria infantum.	+	1–1000	1	17	H	0	+	6–12	+	+	Impr.	Taken home early.
140	Dyspeptic diarrhœa.	0		1.3	17	M & H	0	+	3–12	0	0	Well.	Child convalescent when blood taken.
142	Diarrhœa, simple. Adenitis cervical, tuberculous.	0		3	9	H	0	S[5]	8–11	—[4]	0	Well.	Intermittent simple diarrhœa.
143	Ileo colitis. Dysenteria infantum.	+	1–1000	1	16	H	++	+	7–17	+	0	Well.	Pus in large amount. Positive 31st day also, 1–100.
146	Dysenteria infantum.	+	1–20	1	17	H	0	+	7–10	+	0	Well.	Convalescent when blood taken.
147	Dyspeptic diarrhœa.	+	1–50	1	17	M	0	+	3–7	0	0	Well.	Blood not tried higher. Relapsed.
151	Dysenteria infantum.	+	1–50	1	9	M	+	+	3–7	+	0	Well.	Not tried higher. History blood in stools, slight.
151A	Dysenteria infantum.	+	1–100	3	16	H	+	+	3–12	+	0	Impr.	History blood in stools. None here. Not tried higher. Relapsed.
152	Dyspeptic diarrhœa.	+	1–1000	1	5	M	S	+	4–8	—	0	Impr.	History of 20-30 stools. Relapsed. Vide 237. H+ 1–20 only.
153	Dysenteria infantum.	0		3	10	M	S	+	3–8	+	0	Well.	Suggestive 1–50.
160	Ileo colitis. Dysenteria infantum.	0		3	22	M	+	+	4–19	+	+	Impr.	Pus in stools.
161	Marasmus.	+	1–20	1	20	H	0	+	3–10	—	0	Died.	Negative higher.
162	Dyspeptic diarrhœa.	0		3	15	M	0	+	4–7	0	0	Well.	See No. 285. Relapsed.
163	Dyspeptic diarrhœa.	0		3	15	H & M	+	+	6–8	0	+	Well.	No blood in stools while here.
165	Dyspeptic diarrhœa.	0		3	17	H	+	+	4–8	—	0	Well.	No blood while here. One of twins, other malnutrition.
166	Malnutrition. Dyspeptic diarrhœa.	0		3	15	H	0	+	3–4	0	0	Well.	Negative also later in summer.
167	Dyspeptic diarrhœa.	0		3	10 & 21	H	0	S	6–10	—	0	Well.	
169	Malnutrition. Dysenteria infantum.	0		3	29	H	0	+	3–18	+	0	Well.	Child one of twins, other died at home previously of "summer complaint." See 283. Relapsed.
178	Dyspeptic diarrhœa.	0		3	26	M	0	+	3–7	0	0	Disch. well.	Died at home later.
179	Malnutrition.	0		3	21	H	0	S	3–6	—	0	Died.	Suggestive 1–100
180	Dyspeptic diarrhœa.	0		3	24	H	S	S	3–12	0	0	Well.	History of slight blood, none here. Suggestive 1–20.
183	Dyspeptic diarrhœa.	0		3	24	H	0	+	8–11	0	0	Well.	History 15–20 stools.
185	Ileo colitis. Dysenteria infantum.	00		3	33.61	H.M	+	+	4–12	+	0	Well.	Suggestive 1–100. Pt. convalescent. History 16–24 stools.
187	Dyspeptic diarrhœa.	0+	1–1000	3	8.29	H.M	0	+	3–6	0	0	Well.	Suggestive 1 hr. 1–250
188	Dyspeptic diarrhœa.	0		3	8.29	H.M	0	+	4–11	0	0	Well.	Twin of 187. Suggestive 8th day.
189	Malnutrition. Dysenteria infantum chronica.	+	1–100	3		H	0	0	2–5	—	0	Well.	Acute history of attack in April with isolation of organism. See text.
190	Malaise. Dysenteria infantum chronica.	+	1–250	3		H	0	0	2	—	0	Well.	Acute history of attack in April with isolation of organism. See text.
191	Malnutrition.	0		3	13	H	0	+	2–5	—	0	Well.	
194	Malnutrition. Dyspeptic diarrhœa.	0		3	5	H	0	S	6–10	—	+	Died.	Twin sister of 195.
195	Dysenteria infantum.	0		3	4	H	0	S	4–11	+	+	Impr.	
198	Dyspeptic diarrhœa.	0		3	7	H	0	S	2–5	—	+	Well.	Strongly suggestive 1–100.
200	Dyspeptic diarrhœa.	+	1–1000	1	8	M	+	+	2–8	0	0	Well.	History of very frequent stools.

TABLE I.—*Continued.*

Clinical Number	Clinical diagnosis.	Reaction.	Dilution.	Time of observation.	Day of disease.	Organism.	Blood in stools.	Mucus in stools.	Number of stools in 24 hours.	Bacteriolog. Diag.	Serum given.	Result.	Remarks.
201	Dyspeptic diarrhœa.	0		3	7	H	0	0	2	—	0	Well.	History of 17 stools.
203	Dyspeptic diarrhœa.	0		3	21	H	0	+	2	—	0	Well.	History 6–7 stools. Clinically negative.
204	Dyspeptic diarrhœa.	0		3	3	H	0	+	3–7	0	+	Well.	
209	Dyspeptic diarrhœa.	0		3	11	H	0	+	3–5	—	0	Well.	
210	Ileo colitis. Dysenteria infantum.	0		3	7	H	0	+	3–8	+	+	Died.	
212	Dyspeptic diarrhœa.	0		3	35	M	+	+	4–8	—	0	Well.	Child well when blood taken, day of discharge.
213	Dyspeptic diarrhœa.	0		3	25	M	0	+	4–11	—	0	Well.	Relapsed. See 327.
215	Dyspeptic diarrhœa.	0		3	11	H	0	S	2–4	—	0	Impr.	Died at home.
219	Dyspeptic diarrhœa.	+	1–1500	3	23	M	+	S	3–6	0	0	Well.	History only, of blood. Relapsed. See 287. Suggestive 1–250, 1 hr.
220	Dyspeptic diarrhœa.	00		3	18.25	M	0	+	3–9	0	0	Well.	
221	Ileo colitis. Dysenteria infantum.	0		5	21	H	+	+	4–16	+	+ +	Died.	History of 20 stools. Strongly suggestive 1–100.
222	Dysenteria infantum.	0		3	7	H	0	+	2–6	+	+	Well.	History 10–12 stools. Relapsed.
223	Ileo colitis. Dysenteria infantum.	0		3	26	H	+	+	4–12	+	+ + + +	Died.	Suggestive 1–50.
224	Dyspeptic diarrhœa.	0		3	12	M	0	+	3–5	—	0	Impr.	Convalescent when tested, day of discharge.
228	Dyspeptic diarrhœa.	+	1–500	1	17	M	0	+	2–5	0	0	Well.	
230	Dyspeptic diarrhœa.	+	1–100	3	23	H	+	+	3–8	—	0	Well.	History of blood once. None noted here.
232	Diarrhœa, simple.	0		3		H	0	S	2–3	—	0	Well.	
235	Dyspeptic diarrhœa.	0		3	22	M	0	+	2–5	—	0	Well.	
237	Dyspeptic diarrhœa, relapse.	0		3	17	M	0	+	3–6	—	0	Well.	Child well when blood taken. Relapse. See 152.
239	Dyspeptic diarrhœa.	0		3	19	M	S	+	4–10	0	0	Well.	History of blood once, slight.
240	Dyspeptic diarrhœa, relapse.	+	1–1000	1	18	M	0	+	3–5	—	0	Well.	Relapse. Blood not tried 1st admission.
241	Dyspeptic diarrhœa.	0		3	9	H	+*	+	3–7	—	0	Impr.	Take home early.
243	Malnutrition. Colitis. Bronchopneumonia. Dysenteria infantum.	+	1–1000	3	25	M	+	+	3–8	+	0	Died.	Blood positive 1–250 in 1 hour.
244	Dyspeptic diarrhœa, relapse.	0		3	3	H	0	+	4–16	0	+	Well.	Readmission, No. 148. 3d day relapse.
255	Diarrhœa, simple.	0		3	14	M	0	+	2–4	—	0	Well.	
258	Dysenteria infantum.	+	1–100	1	7	M	0	+	5	+	0	Impr.	Taken home early.
259	Ileo colitis. Dysenteria infantum.	+	1–100	5	30	M	+	+	5–13	+	0	Well.	Negative 3d day, strongly suggestive 1–1000. Probably positive higher than 1–500, but overgrown. Pus in stools.
260	Malnutrition.	0		3	23	M	0	+	2–4	—	0	Well.	Suggestive 1–100.
261	Dysenteria infantum. Suppression of urine.	+	1–1000	1	16	M	+	+	9	+	+	Died.	
263	Dysenteria infantum.	+	1–500	3	40	M	0	+	5–9	+	0	Well.	Taken home early. History 15–20 stools. S. 1–100, 1 hr. S. 1–1500, 3 hr.
264	Dyspeptic diarrhœa.	0		3	28	M	0	+	5–11	—	0	Well.	S. 1–100, 1 hr. Lived in same house with No. 265.
265	Dyspeptic diarrhœa.	0		3	25	M	0	+	4–10	—	0	Well.	History of onset with 35 stools per day.
271	Malnutrition. Dysenteria infantum. Intestinal obstruction.	+	1–1000	1	2	M	0	+	3–8	+	+	Died.	
272	Ileo colitis. Dysenteria infantum. Furunculosis. Glossitis.	+	1–100	1	14	M	+	+	4–12	+	+ + + + +	Unimpr.	Taken home. Died next day.
274	Dysenteria infantum.	+	1–100	3	14	M	0	+	4–8	+	+ + +	Impr.	History 15–20 stools. Taken home. Died.
277	Dyspeptic diarrhœa.	+	1–500	3	39	M	0	S	3–5	—	0	Well.	

TABLE I.—*Continued.*

Clinical Number.	Clinical diagnosis.	Reaction.	Dilution.	Time of observation.	Day of disease.	Organism.	Blood in stools.	Mucus in stools.	Number of stools in 24 hours.	Bacteriolog. Diag.	Serum given.	Result.	Remarks.
278	Malnutrition. Colitis. Dysenteria infantum.	+	1-100	1	14	M	0	+	12	+	++	Died.	History of pus in stools. Suggestive 1–1000, 1 hr. Died day after admission. Probably positive higher.
280	Malnutrition.	+	1–100	3	20	M	0	S	4–5	—	0	Well.	Suggestive 1–500, 1 hr.
281	Dysenteria infantum	0		3	14	M	+	+	3–5	+	0	Well.	History 10–15 stools.
283	Dyspeptic diarrhœa.	+	1–100	3	8	M	0	+	3–8	—	+	Well.	Suggestive 1–250, 3 hrs. Readmission No. 169.
285	Ileo colitis. Dysenteria infantum.	+	1–1000	3	see text 67	M	+	+	4–17	+	+	Died.	Relapse No. 162.
286	Malnutrition.	0		3	36	M	S	+	7–27	0	++	Impr.	
287	Ileo colitis. Dysenteria infantum.	Blood not tried this admission.		See text.			+	+	4–15	+	++ ++	Died.	Blood not taken through oversight. Relapse. See No. 219.
295	Dysenteria infantum.	+	1-100	3	2½ mos.	M	S	+	3–9	+	0	Well.	S. 1–500, 3 hrs. History 10–12 stools.
299	Dysenteria infantum	0		3	26	M	+	+	5–11	+	0	Impr.	Taken home early. Died at home.
301	Malnutrition. Colitis. Dysenteria infantum.	0		3	22	M	+	+	4–7	+	++	Died.	
310	Dyspeptic diarrhœa.	+	1–500	3	16	M	+	+	2–11	—	0	Impr.	History of bloody stools, 10–15 per day. S. 1–1000.
317	Dysenteria infantum.	+	1–1000	1	R. 14	M	+	+	9	+	+	Died.	Relapse. Resembled cholera infantum.
318	Marasmus. Dyspeptic diarrhœa.	+	1–1000	3	24	M	+	+	3–9	—	0	Impr.	Not observed 1 hr.
322	Pyelitis. Malnutrition.	0		3	28	M	0	+	1–5	—	0	Unimpr.	
327	Dysenteria infantum.	+	1–100	3	R. 26	M	0	+	7–17	+	0	Impr.	Accident to high dilutions. Pus in stools. Relapsed. Case No. 213.
328	Rachitis. Dysenteria infantum.	+	1–250	1	19	M	0	+	4–14	+	+	Well.	S. 1–500, 3 hrs. Relapse, No. 316.
330	Ileo colitis. Malnutrition. Dysenteria infantum.	+	1–1000	3	16	M	+	+	5–10	+	+	Died.	Not observed 1 hr.
331	Malnutrition. Rachitis. Dyspeptic diarrhœa.	+	1–1000	3	2 mos.	M	S	+	5–8	0	0	Unimpr.	+ 1–50, 1 hr. Intermittent diarrhœa. S. 1–1000, 1 hr.
332	Dyspeptic diarrhœa.	+	1–1000	3	15	M	0	S	5–11	—	0	Well.	S. 1–250, 1 hr.
333	Ileo colitis. Eclampsia. Dysenteria infantum.	+	1–0000	3	15	M	+	+	17.29 44.	+	++	Died.	Cholera infantum type. Pus in stools. + 1–250, 1 hr.
335	Ileo colitis. Eclampsia. Dysenteria infantum.	+	1–1000	3	10	M	+	+	9–13	+	+	Died.	Muco-pus in + stools. + 1–200, 1 hr.
338	Dysenteria infantum.	+	1–200	3	15	M	+	+	5–9	+	+	Impr.	No blood in stools at Sanitarium. History 10–14 stools.
339	Dysenteria infantum.	+	1–100	1	33	M	0	S	4–7	+	0	Impr.	Taken home. S. 1–250 1 hr. History 8–10 stools.
342	Dyspeptic diarrhœa (convalescent).	+	1–500	3	16	M	0	+	2–5	—	0	Well.	S. 1–1000, 3 hrs.
343	Malnutrition.	+	1–1000	4	28	M	0	+	5–10	0	0	Impr.	
348	Rachitis. Stomatitis. Dyspeptic diarrhœa.	0		3		M	+	+	3–6	—	0	Well.	Sick "off and on". Worse for 3 days.
349	Malnutrition.	+	1–1000	3		M	0	+	6–9	—	0	Impr.	History of intermittent diarrhœa. Died at home.
381	Dyspeptic diarrhœa.	+	1–1000	4	42	M	+	+	6–10	—	0	Impr.	History of blood once only.
383	Dyspeptic diarrhœa (Reinfection.	0		4	7	M	+	+	3–7	—	+	Impr.	History 5–13 stools.

[1] "Mortenson" cultures.
[2] Each + stands for 50 cc. serum or fraction thereof.
[3] "Harris" culture.
[4] — = not examined.
[5] S = slight amount.
"Time of observation" is given in hours. "S" in "remarks" = suggestive. "Taken home" refers to cases taken home by parents against advice, usually early. Day of disease reckoned approximately, i. e., "Child sick about 3 weeks" = 21 days. "Number of stools" gives upper and lower limit of number during attack, before convalescence.
[6] All organisms isolated from stools were of the type producing acid in mannite litmus agar. No alkaline forms were observed.

one reacted 1-20 in convalescence (146). Of the remaining seven cases, one was of only nine days duration, and blood at autopsy reacted 1-50. Of the remaining six cases (15 per cent) only one was over 25 days duration. Of the forty-two cases with a diagnosis of dyspeptic diarrhœa or ileocolitis, fourteen gave a positive reaction; but as no bacteriological examination was made of the stools in very many of the negative cases, there is no certainty that they were all due to infection with *B. dysenteriæ*, though a fairly large number of them were undoubted dysentery cases, blood in stools, etc. Many of them were early cases, and some were positive in low dilutions or suggestive even higher. Whether or not repeated examination of the blood might have changed the result, cannot of course be stated. Of the five cases of malnutrition and marasmus giving a positive agglutination reaction, two (189 and 190) had dysentery in the spring (see below), one had a history of intermittent diarrhœa lasting two or three months, and one had a marked mucus diarrhœa on entrance (343). Of the negative cases, one was positive 1-20 (161), and one was suggestive 1-100 (179).

As regards day of disease upon which a positive reaction was obtained, the earliest was 271 which reacted in a dilution of 1-1000 on the second day, and the next earliest was 123 which gave a reaction in the same dilution on the third day. Other early cases were: 152, 5th day; 258, 7th day; 200, 8th day; and 136, 9th day. Other early cases, but all giving negative reactions, were 194, 195, 198, 201, 204, 210, 222, 241, 244 (3d day of relapse), and 383. With the exception of 201, and 241 who was taken home the next day, all these cases were injected with antidysenteric serum, and hence it was impossible to try their blood reactions later without this new factor being considered. Such cases were not tried again. Many cases however, as late as the twenty-fifth or thirtieth day gave a negative reaction (169, 178, 213, 220, 223, 264, 265, 299), though in two instances (169, 213), such cases later gave a positive reaction when returned with a relapse (283 and 327). No. 162 was negative on June 25, 15th day of disease, but having been sick at home nearly all the time since discharge, returned to the Sanitarium and on July 24, gave a positive reaction 1-1000, and again on August 17 (67th day).

The persistence of the reaction was found to be variable. No. 152 was positive 1-1000 on June 23, 5th day of attack, but when well on July 24, after a relapse, 31st day of disease, her blood was quite negative. No. 146 when convalescent only gave a positive reaction 1-20 on the seventeenth day of disease; here, unfortunately, no earlier examination had been made. No. 212, when well on the thirty-fifth day of a rather sharp attack gave a negative reaction; here, too, no earlier examination had been made. No. 260 was positive 1-500 on the fortieth day while still very sick. No. 277 was positive 1-500 on the thirty-ninth day. No. 331, a child previously fed on condensed milk, and the subject of marked rickets and malnutrition, had been ill off and on for two months or more with mucous diarrhœa, and with a trace of blood in the stools on one or two occasions; he gave a positive reaction 1-1000 in three hours, suggestive 1-1000 in one hour, positive 1-50 in one hour. Here the specific organism was very carefully searched for, but not found. No. 339 was positive 1-100 on thirty-third day. No. 143, positive 1-1000 in one hour on sixteenth day, still gave a positive reaction when discharged on the thirty-first day. Nos. 189 and 190 are especially interesting cases. In April, three months before, they both had an attack of bloody diarrhœa, following a similar case in an adult in their family. *B. Dysenteriæ* was isolated from both children by Dr. Bassett,[2] and their blood reacted positively. They were admitted to the Sanitarium with malaise and malnutrition, but had no diarrhœa; they had had no diarrhœa since April, though in each case blood examination was still positive, 1-100 and 1-250 respectively.

TABLE III.

	Day of disease.																Total
	2	3	4	5	6	7	8	9	10	10-14	14-21	21-28	28-35	35-45	Over 45		
Positive reactions....	1	1*	..	1	..	1	3	.	1	4	13	7	4	3	6		45
Negative reactions...	..	2	1	1	..	5	2	4	2	6	18	13	4	..	5		63
																	108 *

*Some cases tested twice.

The dilutions tried were 1-20, 1-50, 1-100 in all cases; 1-250, 1-500, 1-1000 in most cases; and 1-1500 in a few cases. But one case of those tried 1-1500 reacted positively. Several reacted 1-1000 as is shown in Table IV.

TABLE IV.

Reaction Dilutions.

1-100	13 cases.
1-250	3 cases.
1-500	5 cases.
1-1000	22 cases.
1-1500	1 case.

Of the relationship of diagnosis and day of disease to height of reaction very little can be said, as there seems to be no constant relation in this regard, some mild cases giving positive reactions at high dilutions, and some severe cases giving positive or even negative reactions at low dilutions. The same may be said in regard to the relation between day of disease and the height of reaction. A more marked influence upon the height of reaction was exerted by the degree of seeding of the suspension of the organism; a light seeding reacting oftentimes higher than a heavy one. This is probably due to the amount of agglutinin in the blood serum being insufficient for a large number of organisms. However, a quicker reaction could often be obtained with a heavier seeding. Practically no work was done with a view of determining the relative reactive powers of the different strains of organisms, further than to observe that the culture "Mortenson," an acid type isolated from a case of dysenteria infantum in the summer of 1902, and recently passed through a guinea-pig gave more

[2] My thanks are due to Dr. Bassett for the facts just stated, and the results of the bacteriological examination of stools mentioned in Table I.

satisfactory results than the stock culture of the "Harris" strain isolated by Flexner in Manila. This culture, denoted "M" in the main table, was usually used in making the examination; when not used, a Harris culture was utilized, denoted "H." Our choice of an acid type of the organism for these tests was dependent upon the fact that all the bacilli isolated from the cases at the Sanitarium in 1902 and 1903, were of this type.

Of the 44 positive cases, 23 showed blood in the stools while under observation or gave a history of having had blood. All showed mucus, except 189 and 190 mentioned above, and a few showed pus. Of the 42 cases in the table with blood in the stools, 24 gave a positive reaction, and 18 a negative one, most of the negative cases being very early ones.

No controls with other organisms were made, but several controls with agglutinating serum (immune serum) were made, and in every case controls of the bouillon suspension of the organisms were made and followed with the serum mixture. The clumping was only in a few instances that of the agglutination of the typhoid bacillus, large compact clumps, the clumps usually being much smaller. The small clumps were either compact or loose, generally the former, but the large clumps were often quite loose, the "chain" or "skein" clumps (the end to end agglutination) being several times observed. Free organisms were scarce, absent in the low dilutions, and not frequent in the high ones. Though *B. dysenteriæ* has no true motility, yet the Brownian movements were usually very active, and these were much quieted by the agglutination, if not entirely inhibited. This is regarded as important, and oftentimes when the control suspension was somewhat clumped from overgrowth, or from poor suspension of the organism it was a very helpful, if not a diagnostic point, as active movements of the clumps or of the individual bacilli in them were always seen in the control.

With a few exceptions all reactions were observed at one hour and at three hours; a few were observed at four or five hour intervals. Of the positive cases, eighteen reacted at one hour (this does not show in table, as times there given are for reaction of the highest dilution), and twenty-six at three hours. Many times a positive reaction in low dilutions has been present in one hour, but not until three hours were the higher dilutions positive. Some high dilutions had to be disregarded at the second reading on account of overgrowth (four or five hour readings) and in such cases only the first reading is recorded.

REPEATED COPIOUS HÆMOPTYSIS FROM AN AORTIC ANEURISM, EXTENDING INTO THE RIGHT LUNG AND FINALLY RUPTURING INTO THE PLEURA.[1]

By Thomas Wood Clarke, M. D.,

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Resident Physician, Lakeside Hospital, Cleveland, Ohio.

The case I wish to report is that of J. McD., an Irishman, 39 years of age, who was admitted to the Lakeside Hospital, Medical Number 4303, in the service of Dr. Edward F. Cushing, on July 13, 1904, complaining of pain in the right upper chest, cough, and expectoration of blood. His father had died of consumption. Beyond this the family history was negative. The patient had always been a healthy, strong man, by occupation a laborer, and had done hard work all his life. He had rheumatism twelve years ago, and slight attacks of the same disease ever since then. As to specific history, the patient admitted having gonorrhœa three times, the last attack eight years before, and a soft chancre eighteen years ago. No history of a primary sore or secondary syphilitic lesions could be obtained. Except for the minor diseases of childhood, the patient had had no further illnesses. He used alcohol to excess.

The patient dated his present trouble from a year before admission to the Hospital, when he began to have discomfort in his chest, especially the right front, shortness of breath, dizziness, ringing in the ears, and attacks of weakness. His general condition grew worse until two weeks before admission to the Hospital, when he began to cough and expectorate small amounts of blood. At this time, the pain in the chest grew much more severe, and on admission it extended to the right shoulder and down the right arm to the elbow. On the day he came into the hospital, he had had an especially profuse hæmorrhage, but was quite indefinite as to the exact amount. During the past year, he had lost twenty pounds in weight.

On examination, the patient was found to be a well built, muscular man, coughing frequently and expectorating considerable quantities of blood-stained mucus. His voice was husky but not brazen, and the cough not the typical "goose cough." His respirations were normal, the pulse regular and of good volume, 88 per minute. The left pulse seemed slightly more full than the right. They were synchronous. The face was of good color; pupils equal and normal; slight arteriosclerosis. There was a very slight tracheal tug. On inspection of the chest, it was found to be symmetrical and the expansion equal. Over the first and second right inter-spaces, for a distance of 11 cm. from the mid-line and over the third inter-space for 4 cm., there was a marked visible pulsation,

[1] Read before the Clinical and Pathological section of the Cleveland Academy of Medicine, on Nov. 4, 1904.

but no bulging of the chest. On palpation over the pulsating area a slight systolic impulse could be felt, followed by a marked diastolic impact. There was no thrill. On percussion, dullness was obtained in this region over an area of 11.5 cm. laterally, and 9 cm. vertically downward from the right clavicle. The dullness did not extend to the left of the sternum. In the right back, the dullness extended from a point 3 cm. above the angle of the scapula upward for 8 cm., and included the entire space between the spinal column and the scapula. No pulsation or tumor was noted in the back. On auscultation over the right upper chest could be heard a markedly accentuated diastolic shock, and a loud friction rub, synchronous with the respiration. No bruit was audible. The lungs were elsewhere normal.

The apex of the heart was slightly more to the left than normal, in the fifth interspace 10.5 cm. from the mid-line, and the cardiac dullness 13.5 cm. out, or 4 cm. outside of the nipple. Except for a marked increase in the intensity of the aortic second sound, the heart sounds were normal. The physical examination was otherwise negative.

The unquestioned diagnosis of aneurism of the thoracic aorta was made, and the attempt made to put the patient on a modified Tufnell treatment. He, however, objected so seriously to the dry diet, and so absolutely refused to remain quiet, that this had to be given up. For ten days everything went well. After the second day, the bleeding stopped, and the cough and pain were greatly relieved. On July 23, however, after a sudden movement, the patient commenced coughing, and spat up four ounces of almost pure red blood. This was the beginning of a remarkable series of sixteen hæmorrhages. The next was on July 29, 8 ounces, and from then they occurred as follows: August 2, 12 ounces; August 6, 32 ounces; August 9, 16 ounces; August 11, 36 ounces; August 17, 16 ounces; August 20, 6 ounces; August 21, 20 ounces; August 24, 28 ounces; August 28, 10 ounces; September 2, 4 ounces; September 3, 2 ounces; September 5, 16 ounces; September 13, 8 ounces; and September 14, 7 ounces; in a period of seven and a half weeks a total of 225 ounces or slightly over 14 pints. This was almost pure blood, mixed with very little mucus. The hæmorrhages in each case, coming on after some exertion, as sitting up, or reaching for an article on the floor, lasted only a very few minutes, and accompanied paroxysms of coughing. At no time did he raise any fibrin or blood-clot. The hæmorrhages were in each case stopped by morphia, at times as much as a grain being required. The patient became steadily more pale. The red blood count dropped from 4,864,000 to 2,304,000 and the hæmoglobin from 65 per cent to 38 per cent in the first month after which, owing to an accident to the hæmoglobinometer, no record could be taken, but from the patient's appearance, it must have been much below this. Two days after the last hæmorrhage on September 15, 1904, the patient during a fit of anger, suddenly sat up in bed, became very weak, broke out into a cold sweat, and said he was dying. The pulse rose from 80 to 125 but remained fairly strong. The respirations became labored and finally stopped, the heart continuing to beat for some time after this. The patient died in about twenty minutes. During the last few days of the patient's life, signs of fluid were evident in his right chest, causing flatness at the base. The probable size of the aneurism and the danger of puncturing it made it seem inadvisable to use the exploring needle. Several attempts were made to examine the patient's larynx, but no good view could at any time be obtained.

During the illness, it was a matter of much speculation among the attending physicians why an aneurism, with a perforation large enough to cause such repeated large hæmorrhages, should stop bleeding at all, and not cause an immediate lethal hæmorrhage. The explanation of this is perhaps found in autopsy findings for the records of which, and for aid in summarizing the same, I wish to thank Dr. William T. Howard, Visiting Pathologist, and Drs. D. H. Dolley and J. H. Bacon, Resident Pathologists of the Lakeside Hospital.

AUTOPSY REPORT.

The following abstract is taken from the autopsy protocol:

Autopsy by Dr. David H. Dolley, September 16, 1904, aut. No. 536. The body is that of an adult male, 170 cm. long. Rigor mortis marked. Pupils equal and dilated. The chest is flat, the supra- and infra-clavicular fossæ well marked. There is no bulging or other abnormality of the thorax. The abdomen is scaphoid. The extremities are free from wounds, scars, and deformities. The superficial glands are not palpable.

Thorax.—The sternum, ribs, and costal cartilages are normal. The left lung over-laps the heart to more than the usual degree. The upper lobe of the right lung is the seat of a rather firm mass. The middle and lower lobes are not visible. The right pleural cavity contains 3000 cc. of dark blood-tinged fluid containing flakes of fibrin. The right parietal pleura is smooth and free from adhesions. The left pleural cavity contains a small amount of clear fluid. The pleura is smooth and free from adhesions. The thoracic contents were removed en masse.

Heart.—The pericardial cavity contains 200 cc. of clear fluid. The parietal layer of pericardium is somewhat thickened, as is the visceral layer over the right ventricle. At the latter point, the epicardium is red and rough. The pericardium is adherent to the upper lobe of the right lung, over the surface of which it extends for a considerable distance. The heart muscle on section is pale and flabby. The segments of the mitral valve are moderately thickened. The segments of the aortic valve are normal in appearance and show no thickening. The tricuspid and pulmonary orifices are of normal size and appearance. The right auricle is markedly compressed by the aneurism to be mentioned later. All the valves are apparently competent.

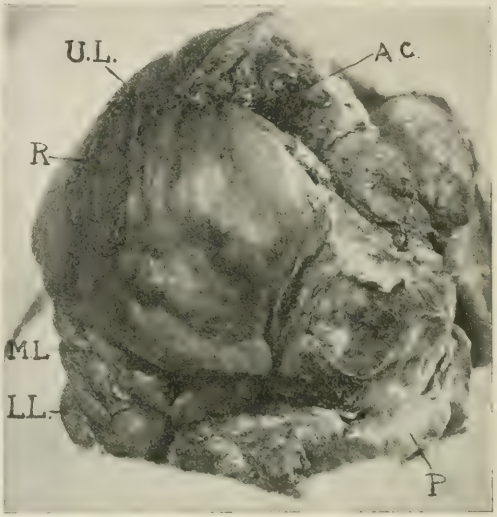
The Aorta.—The aorta just above the valve measures 7.5 cm. in circumference, at the junction of the ascending and transverse portions of the aorta, 8 cm. Below this, the vessel is not dilated. The aorta throughout is the seat of a number of large and small irregular thickened areas, which project slightly into the lumen. Some are calcified and rough. The

large branches of the aorta are normal. On the right side of the aorta, 3 cm. above the valve, there is an oval opening, 2.5 by 1 cm. in diameter, leading into a spherical sac, 9 cm. in diameter, which is filled with laminated fibrin, the superficial layers of which, are soft and of a grayish-red color, while the deeper layers are white and firm. The opening of the sac into the aorta is partly closed by a rather firm mass of grayish-white thrombus. This aneurismal sac, which is round in outline projects upward and somewhat backward, directly into the upper lobe of the right lung, which incases it throughout two-thirds of its extent. Anteriorly the sac is adherent to, and is covered, to a considerable extent, by somewhat thickened pericardium. The walls of the aneurism are comparatively thin, being thickest at the base, where they average 8 mm. and thinnest at the point just opposite the opening into the aorta, at which point the walls are lost in the lung tissue. Over a large part of its extent, the walls of the sac and the visceral pleura are continuous. Microscopically, the wall consists of firm fibrous tissue, organising fibrin and inflamed pleura, with occasional scattered traces of markedly compressed alveoli. At the point directly opposite the communication between the aorta and the aneurismal sac, there is an opening between the latter and the pleural cavity. At this point, the pleura is ruptured, and a rough mass of grayish-red fibrin projects into the pleural cavity. This opening is a linear tear, 5 cm. long. Adherent to the upper lobe of the lung, near this point, there is a fresh blood clot, weighing 700 grams. On transverse section through the sac and the right lobe, the whole interior of the sac is filled with, at some places firm, and at other places friable, clot. The aneurism occupies nearly the whole of the upper lobe of the right lung, and two-thirds of the extent of the aneurism is situated in this lobe. The bronchi leading to the upper lobe contain no blood, but on section, small bronchi can be traced into the aneurism sac. The lower and middle lobe of this lung are collapsed, airless and rather firm. The pulmonary arteries are normal throughout.

The Left Lung.—The left lung is voluminous and markedly emphysematous. On section, it is œdematous throughout. The bronchi of both lungs, the trachea, and larynx are normal in appearance.

Abdomen.—The abdominal muscle and subcutaneous tissue are normal. The diaphragm on the right side projects 4 cm. below the costal margin. The liver is displaced downward and to the left, and reaches a point 5 cm. below the umbilicus, the right lobe lying directly in the middle line. The stomach is displaced downward into the left iliac fossa. The ileum and jejunum and the transverse colon are displaced into the pelvis. The other abdominal organs are in their usual positions. The abdominal cavity contains a moderate amount of clear fluid. The peritoneum is smooth and free from adhesions. The liver is of ordinary size and shape. The biliary system is normal. The spleen, kidneys, pancreas, stomach, intestines, and other organs show no pathological changes.

Anatomical Diagnosis. Arterio-sclerosis of the aorta with sacular aneurism of the ascending arch of the aorta, projecting into and occupying a greater portion of the upper lobe of the right lung. Compression atelectasis of the right lung. Ruptured aneurism and extensive hæmorrhage into the right pleural cavity. General enteroptosis. Pressure upon the right auricle. Œdema and chronic passive congestion of both lungs. Hydro-thorax, hydro-pericardium, and hydro-peritoneum. Communications between aneurism and small bronchi.



Right Lung Showing Aneurism.

U. L. = Upper Lobe and aneurism. M. L. = Middle Lobe. L. L. = Lower Lobe. A. C. = Aneurism Cavity opened. R. = Rupture. P. = Pericardium.

LITERATURE.

The point of especial interest raised by this case is that of non-lethal hæmorrhages in cases of thoracic aneurism. After looking up with some care, all the literature available in Cleveland, I have been compelled to conclude that such cases are very rare. Though cases have occurred, in which one or two severe hæmorrhages have been followed by months or even years of exemption, I have not found reference to any such series of large hæmorrhages as are here reported. With the facilities at my disposal, I have been unable to make a complete review of the literature, but have collected six cases showing one or more points of similarity to the present one.

In 1847, the case of the English surgeon, Mr. Liston was reported. This gentleman, after one profuse hæmorrhage, was absolutely well for three months. Then, after two months in which he steadily failed, and expectorated considerable rusty sputum, he died, without further hæmorrhage. At autopsy were found three old perforations into the trachea, blocked by blood clot. (1)

Gairdner, in 1859, reported a case in which the patient was ill ten years. Four years before he died, he had two profuse

hæmorrhages from his lungs, followed by some staining of the sputum. After this, he had no more hæmorrhages, though for the last six months, some staining, until a hæmorrhage of eight ounces caused suffocation and death. The autopsy revealed an aneurism of the descending aorta which had perforated the left bronchus and trachea, the perforation being filled with old clot. The left lung was collapsed but not involved. (2) Gairdner also states that up to that time, 1859, nine cases of thoracic aneurism had been reported which had had hæmorrhage two months or more before death. He gives no references except to the case of Mr. Liston, and I have been unable to find these cases.

Two cases are reported by Dr. Osler somewhat similar. The first, in which the patient had a hæmorrhage of two quarts and three weeks later slight hæmoptysis, Dr. Osler reports eight months later as a cured aneurism. (3) The second is a man, who, after one profuse hæmorrhage, lived four weeks, and then dropped dead without further bleeding. At autopsy, this case was very similar to the one here reported. It was an aneurism of the ascending arch, a large part of the wall of which was made up of pulmonary tissue, the trachea not being involved. In this case, as in the present one, death followed perforation of the aneurism into the right pleural sac, with internal hæmorrhage. (4)

Peacock reported in London still another case where the descending arch was involved, the aneurism wall being composed of the upper lobe of the left lung. This case spat up small amounts of blood for some time and finally died from rupture into the left pleura. (5)

Involvement of the lung in aneurism is a comparatively rare occurrence, but is one thing to be thought of in the consideration of pulmonary hæmorrhage, especially where there is a suspicion of thoracic aneurism. That an aneurism may cause extensive destruction of lung tissue without hæmorrhage is shown by Johnson's case. In this, the patient had symptoms of chronic pleurisy, and had no hæmorrhage until the fatal one. Aneurism was not suspected, but at autopsy one was found, of the descending aorta involving the lower left lobe of the lung, the aneurism walls being only one quarter of an inch thick, composed of fibrin, indurated lung and pleura. (6) This of course, must have existed for some time, but the bronchi were presumably compressed and obliterated in the wall of the sac.

From the above cases it would appear that, while hæmoptysis is a common fatal termination in thoracic aneurism, a very large hæmorrhage may occur in this disease, without causing the death of the patient, and that occasionally a patient may have one or more large hæmoptyses, and finally die from some other complication of the aneurism. The point of bleeding may be from rupture into the trachea or bronchi and be stopped by the opening being plugged with fibrin, or it may occur from involvement of the lung tissue itself. In the latter case, it is probable that the small bronchioles open into the wall of the sac, but are so compressed by it, that they normally remain closed, or are covered by fibrin. On exertion, or moving, either the fibrin shifts its position, or the straining of coughing opens the ends of the small bronchi and the blood leaks out. On the patient again becoming quiet, either naturally or by means of narcotics, the original condition is resumed and the bleeding is temporarily arrested.

In closing, I wish to express my thanks to Dr. William Osler of Baltimore, for some useful suggestions and for information concerning his cases, and to Dr. Edward F. Cushing of Cleveland for permission to report this case from his service at the Lakeside Hospital.

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(4) Ibid., 1889, XIX, p. 223.
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(6) Lancet, London, January 12, 1867, p. 44.

A CASE OF CÆSAREAN SECTION FOLLOWING VENTRAL FIXATION.

By Alfred Hull Clark, M. D., and Robert Lee Bowley, M. D.,
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In a recent number of the Bulletin, Dr. Lynch published an analysis of a series of cases of Cæsarean section necessitated by ventral fixation of the uterus. To this the following case treated at the Hartford Hospital may be added.

J. I. (No. 36,541), white, aet. 39, was admitted May 3, 1904. She began to menstruate when she was fourteen and her periods had always been regular and the flow moderate in amount during the three days it generally lasted. She was married at twenty, but had no children. In July of 1901, she entered the Hartford Hospital with a history of painful defecation during the previous four or five years. A diagnosis of a malignant tumor pressing on the rectum had been made before her entrance, but on examination the trouble was found due to a retroverted uterus. This was fixed firmly to the anterior abdominal wall and her symptoms were relieved.

In the spring of 1903, she was married again. She became pregnant, her last sickness dating from July 15, 1903, and had a comfortable, normal pregnancy with no œdema, headache, or morning-sickness. She re-entered this Hospital, May 3, 1904. She had expected her confinement April 22. At the time of her entrance she was in no pain.

A physical examination showed a slender, rather poorly

nourished woman. Head, heart and lungs were negative. The abdomen was fairly symmetrically enlarged, the umbilicus was flat and the lineæ striæ were not numerous. The position of the child could not be made out by external palpation, the palpable parts being very confusing and the abdominal walls tense. The fœtal heart was heard 5 cm. above the navel in the median line. The cervix could not be reached per vaginam until a small hand was introduced when it was felt above the promontory of the sacrum and well back toward the spinal column.

Pelvic measurements: Between anterior-superior spines, 27 cm.; between iliac crests, 28 cm.; Baudelocque's diameter, 18 cm.

Upon May 4, the head of the child was thought to be in the left upper quadrant of the abdomen. With the patient under chloroform version was tried, one physician manipulating the fœtus externally and a second with his hand in the vagina. The child could not be turned. After the manipulations there was slight bleeding from the vagina which continued until she was delivered two days later. The night was passed comfortably, but during the night of May 5, she was very uncomfortable and restless though there were no typical labor pains.

May 6, at 1 p. m. the os was found dilated about 2.5 cm. and at 4 p. m. it was almost fully dilated. The patient had constant pain in back and groins. Late in the afternoon internal version was decided upon and attempted, but on introducing the hand into the uterus to grasp a foot a shelf of tissue was found on its anterior wall which much impeded any search for parts though the position of the head was recognized. Upon further examination the bowel was found prolapsed into the uterus. The diagnosis of a ruptured uterus led to her hasty transfer to the operating room.

On opening the abdomen the uterus was found ruptured in its very much thinned posterior wall and a dead, hydrocephalic fœtus was found lying half in the uterus and half in the peritoneal cavity. The uterus was amputated from the cervix, freed from its attachment to the anterior abdominal wall and removed together with its appendages. The peritoneum was sutured over the stump and the abdominal wall was closed in layers.

The patient was comfortable the next morning, but in the afternoon complained of pain in the abdomen and about 6 p. m. developed a maniacal excitement that necessitated restraint by a sheet. The mania was of extreme violence and once she caught her tongue between her teeth and bit it until it was cyanotic. This disturbed condition lasted until the morning of May 8, when she gradually regained her normal mental status and from that time made an uneventful recovery except for a slight stitch abscess and a profuse, purulent, vaginal discharge which, however, soon cleared up under bichloride douches.

The fundus of the uterus was found firmly fastened to the anterior abdominal wall by a broad area of adhesions which allowed no motion whatever. The anterior wall and fundus of the uterus were very much thickened and the anterior wall so sharply bent upon itself that its upper segment formed with its lower an acute angle which made the shelf of tissue felt per vaginam. The posterior wall was very much stretched and thinned out and was ruptured enough to allow part of the fœtus to prolapse into the abdominal cavity and bowels into the uterus. The rupture probably occurred at the time of the attempted external version.

A SURVEY OF OVARIOTOMY AT EXTREMES OF LIFE. REPORT OF A CASE IN A GIRL AGED 5.[1]

By Harry I. Wiel.

The occurrence in the service of Dr. Howard A. Kelly at the Johns Hopkins Hospital, of an ovariotomy in a girl 5 years old, has afforded the raison d'etre of a survey of the cases reported in literature suggesting not only a consideration of the subject in relation to the very young, but by way of contrast, also in the aged. It is not the purpose of this article to go into the pathological and clinical aspects of the subject in detail, as the writings of Hennig, Homans, Kelly, and Bland Sutton consider in full that side of the question. Here is meant rather to emphasize by statistics the frequency of occurrence of the various tumors of the ovary and the results of ovariotomy.

That all of us realize the plasticity of statistics, is true. The Germans put it very aptly when they say "Papier ist geduldig," and that note of warning should be sounded in the interpretation of these. We have taken the statistics as we found them, and when the percentage of recoveries is noted it must be borne in mind that many of the cases were reported solely because there was recovery, while it may be assumed that some cases with unfavorable issue are unrecorded. Furthermore, many of the reporters mean by recovery, merely immediate recovery, though death (as happened in some cases) occurred from metastasis of the tumor. These remarks apply more particularly to the cases in the young than those in the old, for the reason that the after histories of the latter have been followed more extensively, and that when death did occur, circumstances of age determined the cause to be something entirely foreign to the ovarian condition.

Under the term "extremes of life" we have arbitrarily fixed

[1] Presented before the Johns Hopkins Hospital Medical Society, December 19, 1904.

the limits of 10 years of age and under, and 70 years of age and over. The story of ovariotomy at these ages has been told before, and those who have told it have come to definite conclusions.

Garrigues speaks thus: "The age of the patient need not be taken into consideration; ovariotomy has been performed with success in young children and in old women over 80 years of age." Baginsky, though less enthusiastic, says: "Ovariotomies in young children are frequently performed, even with cures. Prognosis becomes better every day as technique of operations in this region progresses." Kelly expresses himself that "The age of the patient does not, as one would suppose, contribute any valid reason for refusing to operate. . . . On account of the large percentage of malignant tumors (in children) and the consequent dangers of delay the operation should be performed as soon as the patient can be suitably prepared for it. The best tonic relief is afforded by the removal of the growth." Even Hennig whose article appeared in 1878, recognized the advantage of early operation in children.

The story in old age does not differ. There seems to be a consensus of opinion among those who have had to deal with the matter, that the extreme age of the patient offers no contraindication whatever. Kelly and Sherwood came to the conclusion that the indications and contraindications in old age are the same as in general operations. They quote Skene Keith, whose emphasis and enthusiasm can best be appreciated in his personal communication, "We like old women to operate on; they always do well." Homans, who from his wide experience gave a large list of ovariotomies, was extremely impressed with the good result in this class of cases, and Bland Sutton, though pessimistic on many subjects, gives a list of 11 ovariotomies in women over 80, all recovering, a result truly remarkable.

It is Bland Sutton, however, who speaks unfavorably of ovariotomy in young children. In the cases he collected (these included 15 years of age and under), dermoids and cysts did well, but in operations for sarcomata of the ovary the results were disastrous. Of his 21 cases of ovarian sarcomata, 11 were dead one year after the operation, a percentage of 52.3 per cent.

Kelly expresses the state of affairs best, viz.: that operation on children under 4 years of age is attended by a mortality of more than one-half of the cases; but on the other hand the results obtained in the older children are remarkably favorable. One would think that the cause of this might be the increased frequency of malignant tumors in the younger years, and Dr. Kelly was of that opinion, but as will be seen by the tabulations below, such is not the case, the malignant tumors being hardly in higher percentage under 5 years of age than between 5 and 10 years.

Dr. Kelly's results were in some degree similar to those of Bland Sutton, and for the sake of comparison, their findings are here given in tabulated form.

	Cysts[2]		Dermoids		Solid Tumors	
	cases	mortality	cases	mortality	cases	mortality
Kelly	43.6%	7.2%	37.2%	21.2%	19%	33.3%
Sutton	41	7.3	38	13.1	21	52.3

These figures, as well as those to follow, are based only upon operated cases. There can be found in the literature, frequent mention of tumors of the ovary, in autopsy cases, and among these one can find instances occurring even in fœtal life. Von Franqué reports such a case. Olshausen reports an autopsy case of carcinoma of the ovary in a girl 8 years old, and another is reported by Amann, where merely an exploratory incision, and not an ovariotomy was done.

The youngest operated case is that of Chiene's, the patient being 3 months old. The result in this case is not known, as the after history is not reported. The child left the hospital however, with the wound healed. The oldest case is that of Thornton's, the patient being of the extreme age of 94. Here there was recovery. More remarkable, however, is the case cited by Owen. He operated on the patient in her 79th year for a parovarian cyst with successful result. In her 86th year she submitted to a second operation for an ovarian cyst of the same side. This was so successful that when seen 4 months after, the patient looked, to quote Owens, "as though she would live to be 100."

The Johns Hopkins Hospital has had some experience in cases of this character, and the results are gratifying. Six ovariotomies in women over 70 are on record, the mortality being nil. All of the tumors were cystic, 3 multilocular and 3 unilocular, 1 of the latter being carcinomatous. Of this number, 5 are reported by Dr. Kelly, the other by Dr. Schenck.

A statistical study of the cases on record here follows:

[2] Under the heading *cysts*, Sutton includes "cysts and adenomata." In the mortality of Sutton's cases of solid tumors, which were sarcomata, 4 of the cases counted here as deaths, recovered from the operation, but died later of metastasis.

CASES 5 YRS. OF AGE AND UNDER.

REPORTER.	AGE.	TUMOR.	RESULT.	REFERENCE.
Chiene	3 mos.	Cyst.	?	Edinburgh Med. Journal, June, 1884.
Power	4 mos.	Cyst.	Recovery.	Brit. Med. Journal, March 5, 1895.
Roemer	1¾ yrs.	Teratoma.	Recovery.	Deutsche Med. Woch., Dec., 1883.
Harris	1⅝ "	Sarcoma.	Recovery.	American Journal of Obstetrics, Oct., 1904.
Péan	2 "	Dermoid.	Recovery.	Clin. Chir., 1887-8.
Busch-Olshausen	2 "	Dermoid.	Death.	Pitha-Bill.
Gibb	2½ "	Cystic Sarcoma.	?	Glasgow Med. Journal, ix, No. 1, p. 33.
Evers	2½ "	Sarcoma.	?	St. Louis Courier of Med., Aug., 1884.
Hooks	2½ "	Dermoid.	Death.	Amer. Jour. of Obstetrics, xix, 1022.
Neville	2¾ "	Dermoid.	Death.	Obstetrical Journal of Great Britain, viii.
Hoffman	2¾ "	Sarcoma.	Death.	Amer. Jour. of Obstetrics, xxxvi.

CASES 5 YRS. OF AGE AND UNDER.—*Continued.*

REPORTER.	AGE.	TUMOR.	RESULT.	REFERENCE.
Alcock	3 yrs.	Multilocular Cyst.	Death.	Lancet, 1871, vol. ii.
Cameron	3½ "	Sarcoma.	Death.	Glasgow Med. Journ., 1889.
Kalb	3⅝ "	Dermoid.	Death.	Medical Sentinel, March, 1897.
Boldt	4 "	Cyst.	Death.	Proc. Path. Soc. of N. Y., 1888.
Schwartz	4 "	Adeno-Cystoma.	Recovery.	Archiv für Gynec., xiii, 4.
Thornton	4 "	Dermoid.	Recovery.	Med.-Chir. Trans., viii, 4.
Foerster	4½ "	Sarcoma.	Death.	Amer. Jour. Obst., xxxi.
Byford	4⅔ "	Sarcoma.	Recovery.	Chicago Med. Record, 1891-2, ii.
Bangs	4¾ "	Multiloc. Cyst.	Recovery.	Amer. Gynec. and Obst. Journ., 1896.
Simons	4¾ "	Papillomatous Cyst.	Recovery.	Virginia Medical Semi-Monthly, Mar. 22, 1901.
Johnson	5 "	Cyst.	Recovery.	Lancet, 1897, i, p. 1093.
Syme	5 "	Cyst.	Recovery.	Australian Med. Journ., xv, 442.
Péan	5 "	Dermoid.	Recovery.	Clin. Chir., 1887-1888.

CASES 6-10 YRS. OF AGE.

Page	6 yrs.	Sarcoma.	Recovery.	Lancet, Dec., 1895.
Lucas	7 "	Mult. Cystoma.	Recovery.	Trans. Clin. Soc., London, xxi, 224.
McKee	7 "	Dermoid.	?	Univ. Med. Magazine, Phil., 1900.
Hamaker	7 "	Mult. Cystoma.	Recovery.	N. Y. Med. Jour., Sept., 1889.
Dandois	7 "	Dermoid.	Recovery.	"Pediatrics," Dec., 1896, p. 520.
Barker	7 "	Dermoid.	Recovery.	Phil. Med. Times., Nov., 1874.
Croom	7 "	Sarcoma.	Recovery.	Edinburgh Med. and Surg. Journal, 1893, p. 689.
Owens	7 "	Dermoid.	Recovery.	Sutton: Surg. Diseases of Fall. Tubes and Ovaries.
Thornton	7 "	Dermoid.	Recovery.	Brit. Med. Jour., 1881, vol. ii.
Chenoweth	7⅔ "	Mult. Cystoma.	Recovery.	Amer. Journ. Obstetrics, xv.
Cupples	7½ "	Dermoid.	Recovery.	Richmond and Louisville Med. and Surg. Jour., Dec., 1879.
Black	7½ "	Dermoid.	Recovery.	British Med. Jour., 1874, vol. i.
Stolypinsky	8 "	Carcinoma.	?	Revue de Gynecologie et de Chir. Abdom., viii, 708.
Dawson	8 "	Papillomatous Cyst.	Death.	Virginia Medical Semi-Monthly, March, 1901, p. 680.
Spencer Wells	8 "	Dermoid.	Recovery.	British Med. Jour., 1874, vol. i.
Omori and Ikeda	8 "	Dermoid.	Recovery.	Berl. Klin. Woch., 1890, No. 7.
Chenoweth	8 "	Sarcoma.	Recovery.	Amer. Jour. of Obstetrics, vol. xv.
Gussenbauer	8 "	Carcinoma.	Recovery.	Wiener Med. Wochenschrift, 1894, No. 47.
McKenzie	8½ "	Dermoid.	Recovery.	Dublin Jour. of Medical Science, 1888, lxxxvi.
Duchamp	8½ "	Cyst.	Recovery.	Arch. de Tocol., 1884, p. 23.
Parkes	9 "	Cyst.	Death.	Amer. Jour. of the Med. Sciences, 1890, p. 258.
Deletrez	9 "	Dermoid.	?	Annales de l'Inst. Chir. de Brux.
Routier	9 "	Dermoid.	Death.	Rev. Gén. de Clin. et de Ther., 1895.
Polotebnow	9 "	Dermoid.	Recovery.	Centralblatt f. Gyn., 1887, i.
Malins	9 "	Cysto-Sarcoma.	Death.	Lancet, 1890, i, 1174.
Forbes	9 "	Myxo-Sarcoma.	Recovery.	Australian Medical Journ., Melbourne, 1894, xvi.
Leopold	9 "	Carcinoma.	Death.	Centralblatt f. Gynekologie, 1894, xviii.
Péan	10 "	Mult. Cystoma.	Recovery.	Arch. de Toc. et de Gyn., 1893, p. 580.
Vincent	10 "	Cyst.	Recovery.	Lyon Méd., lxxiii.
Omori and Ikeda	10 "	Dermoid.	Recovery.	Central. f. Gyn., xvi.
McBurney	10 "	Sarcoma.	Recovery.	Ann. of Surgery, Phil., 1895, xxi, 706.
Wagner	10 "	Sarcoma.	Recovery.	Ann. f. Klin. Chir., xxx, 704.
Meigs	10 "	Cyst.	Recovery.	Boston Med. and Surg. Jour., cxli, p. 316.
Fenomenow	?	Sarcoma.	Death.	Rev. de Gyn. et de Chir. Abdominale, 1904, vol. viii, p. 708.
Karcewski	10 "	Dermoid.	Recovery.	Centralblatt f. Gyn., 1904, No. 17.
Baldy	10½ "	Papillomatous Cyst.	Recovery.	Amer. Gyn. and Obst. Journ., 1899, xiv, 184-186.

CASES 70 YRS. OF AGE AND OVER.

Homans	70 yrs.	Mult. Cyst.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii, 532.
Homans	70 "	Mult. Cyst.	Recovery.	Ibid.
Kaltenbach	70 "	Mult. Cyst.	Recovery.	Ibid., p. 530.
Keith (Skene)	70 "	Cyst.	Recovery.	British Med. Journ., 1887, i, 271.
Hall	70 "	Solid Tumor.	Recovery.	Cincinnati Lancet-Clinic, 1887, xix, 1-4.
Hennig	70 "	Mult. Cyst.	Recovery.	Inaugural Dissertation, Leipzig.
Homans	70 "	Mult. Cyst.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii, 528.
Eastman	70 "	Mult. Cyst.	Recovery.	Ibid., p. 524.
Edwards	70 "	Mult. Cyst.	Recovery.	Ibid.
Fehling	70 "	Mult. Cyst.	Recovery.	Ibid.
Freund	70 "	Cyst. (Cancerous?).	Death.	Records of Frauenklinik der Universität, Strassburg.
Frommel	70 "	Mult. Cyst.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii.
Davis	70 "	2 Colloid Tumors.	Death.	Ibid., p. 542.
Eastman	70 "	Mult. Cyst.	Recovery.	Ibid., p. 524.
Cluness	70 "	Cyst.	Death.	Trans. Med. Soc. of California, 1872-73, p. 48.
Croom	70 "	Mult. Cyst.	Death.	Trans. Edinburgh Obstetrical Society.
Croom	70 "	Parovarian Cyst.	Death.	"Analysis of 100 Cases of Abdominal Section," Edin. Med. Journ., May, 1889.
Bantock	70 "	"Tumor."	Recovery.	Brit. Gynec. Journ., May, 1892, p. 17.
Barnes	70 "	Cyst.	Recovery.	"Ovariotomy in Aged People," Provincial Med. Journ., Apr., 1888.
Van der Veer	70 "	Multiloc. Cyst.	Recovery.	Transactions of Med. Soc. State of New York, 1888; Annals of Surgery, May, 1888.

CASES 70 YRS. OF AGE AND OVER.—*Continued.*

REPORTER.	AGE.	TUMOR.	RESULT.	REFERENCE.
Wells	70 yrs.	"Tumor."	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, vol. iii, p. 549.
Werth	70 "	Mult. Cyst.	Recovery.	Ibid.
Werth	70 "	Mult. Cyst.	Recovery.	Ibid.
Tait	70 "	Cyst. (both ovaries).	Recovery.	British Med. Journal, 1886, i, 923.
Thornton	70 "	"Tumor."	Recovery.	Med.-Chir. Trans., lxxi, 1887, 57.
Thornton	70 "	Carcinoma (both ovaries).	Death.	Ibid.
Sims	70 "	Cyst.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, vol. iii, p. 536.
Sims	70 "	Mult. Cyst.	Recovery.	Ibid.
Reamy	70 "	———	——	Ibid., p. 542.
Roberts	70 "	Mult. Cyst.	Recovery.	Medical Chronicle, Manchester, Oct., 1892.
Meredith	70 "	"Tumor."	Recovery.	"Report of 104 Ovariotomies," Med.-Chir. Transactions, lxxii, 50.
Morison	70 "	Mult. Cyst. (papillomatous).	Recovery.	Lancet, Jan. 21, 1893.
Löhlein	70 "	Fibroma.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii, 530.
Lomer	70 "	Mult. Cyst.	Recovery.	Ibid.
Martin	70 "	Mult. Cyst.	Death.	Ibid., p. 532.
Van der Veer	71 "	Mult. Cyst.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, vol. iii, p. 540.
Werth	71 "	Mult. Cyst.	Recovery.	Ibid.
Thornton	71 "	Papilloma (both ovaries).	Recovery.	Med.-Chir. Transactions, lxx, 1887, p. 64.
Savage	71 "	Mult. Cyst.	Recovery.	Records of Women's Hospital, Birmingham.
Schroeder	71 "	———	——	Berl. Klin. Woch., 1879, i, p. 2.
Sims	71 "	Dermoid.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, vol. iii, p. 536.
Peugnet	71 "	Cyst.	Recovery.	New York Med. Jour., xxiv, p. 191.
Martin	71 "	Cyst.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii, p. 536.
Kelly	71 "	Cyst.	Recovery.	Amer. Jour. of Obst., xxxiv, No. 2, 1896.
Homans	71 "	Sarcoma.	Death.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii, 532.
Bantock	71 "	"Tumor."	Recovery.	"On Hyperpyrexia after Listerian Ovariotomy," Med.-Chir. Trans., lxiv.
Wilson	72 "	Cyst.	Death.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii, 540.
Sims	72 "	Mult. Cyst.	Death.	Ibid., p. 536.
Rheinstädter	72 "	Cancerous Cyst.	Death.	Ibid.
Sänger	72½ "	Mult. Cyst.	Recovery.	Ibid.
Mundé	72 "	Mult. Cyst.	Recovery.	Ibid., p. 534.
Morison	72 "	Mult. Cyst. R. ovary. Fibroma, L. ovary.	Recovery.	Lancet, 1893, Jan. 21.
Martin	72 "	Mult. Cyst.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii, p. 532.
Kelly	72 "	Mult. Cyst.	Recovery.	Amer. Jour. Obst., xxxiv, No. 2.
Homans	72 "	Mult. Cyst.	Death.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii, p. 528.
Homans	72 "	Mult. Cyst.	Recovery.	"Laparotomies."
Gerster	72 "	Mult. Cyst.	Recovery.	Results of Aseptic and Antiseptic Surgery, 1st Edition, 1888, p. 141.
Frommel	72 "	Papillary Cyst.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii.
Cutler	72 "	Mult. Pap. Cyst.	Recovery.	Hospital Records, Waltham, Mass.
Barnes	72 "	Cyst.	Recovery.	British Gynec. Jour., Aug., 1892, p. 159.
Zweifel	73 "	———	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii, p. 540.
Werth	73 "	Cyst.	Recovery.	Ibid.
Werth	73 "	Mult. Cyst.	Recovery.	Ibid.
Staude	73 "	Cyst. (both ovaries).	Recovery.	Ibid.
Söderbaum	73 "	Mult. Cyst.	Recovery.	Eira, Göteborg, 1882, vi, p. 69.
Maury	73¾ "	Cyst.	Recovery.	Mississippi Valley Medical Monthly, 1885, 5.
Kelly	73 "	Carcinomatous Cyst.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii.
Litzmann	73 "	Cyst.	Recovery.	Ibid.
Homans	73 "	Solid Tumor.	Recovery.	Ibid.
McCann	73 "	Fibroma.	Recovery.	Brit. Med. Journal, 1903, i, 127.
Keith	73 "	"Tumor."	Recovery.	Ibid., 1887, ii, 592.
Homans	73 "	Mult. Cyst.	Recovery.	"Laparotomies."
Homans	73 "	Cyst.	Recovery.	Ibid.
Homans	73 "	Mult. Cyst.	Death.	Ibid.
Crooker	73 "	Mult. Cyst.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii, p. 522.
Brennecke	73 "	Mult. Cyst.	Recovery.	Ibid., p. 520.
Balls-Headley	73 "	Dermoid.	Recovery.	Ibid.
Peterson	74 "	Cyst.	Recovery.	Ibid., p. 540.
Martin	74 "	Cyst.	Recovery.	Ibid., p. 532.
Spiegelberg	74 "	———	——	Olshausen, p. 394.
Noble	74 "	———	——	Monthly Homœopathic Review, London, 1903.
Morison	74 "	Mult. Cyst.	Recovery.	Lancet, Jan. 21, 1893.
Kelly	74 "	Mult. Cyst.	Recovery.	Amer. Jour. Obst., xxxiv, No. 2.
Kaltenbach	74 "	Parovarian Cyst.	Death.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii, 530.
Hoffmeier	74 "	Mult. Cyst.	Recovery.	Ibid.
Boldt	74 "	Mult. Cyst.	Recovery.	Ibid.
Croom	74 "	Cyst.	Recovery.	Trans. Edinburgh Obst. Society.
Carmichael	74 "	Mult. Cyst.	Recovery.	New England Med. Gazette, Apr., 1888, p. 119.
Martin	75 "	Tuberculosis.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii.
Kelly	75 "	Mult. Cyst.	Recovery.	Ibid.
Davies	75 "	Cyst.	Recovery.	Brit. Gynec. Journal, 1887, iii, 414.
Croom	75 "	Mult. Cyst.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii.
*Bennett, E. and C...	75 "	Mult. Cyst.	Recovery.	American Medical Times, N. Y., Aug., 1861, iii, 86.
Wilson	76 "	Papilloma.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii.
Josephson	76 "	Glandular Cyst.	Recovery.	Föhr-Svenska, 1889, Kelly and Sherwood.

* First case reported.

CASES 70 YRS. OF AGE AND OVER. *Continued.*

REPORTER.	AGE.	TUMOR.	RESULT.	REFERENCE.
Holland	76 yrs.	Mult. Cyst.	Recovery.	Brit. Gynec. Jour., vii, 179.
Croom	76 "	Papilloma.	Recovery.	Records of Edinburgh Royal Inf.
Croom	76 "	Mult. Cyst.	Recovery.	Ibid.
Winkel	77 "	Cyst. R. ovary. Mult. Cyst. L. ovary.	Recovery.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii.
Wilcke	77 "		Recovery.	Olshausen, p. 394.
Wells	77 "	"Tumor."	Death.	Med.-Chir. Transactions, lx.
Terrier	77 "	Fibroma (both ovaries).	Recovery.	Progrès Medical, 1888, p. 466.
Morison	77 "	Mult. Cyst.	Recovery (?).	Lancet, Jan. 21, 1893.
Mann	77 "	Mult. Cyst.	Recovery (?).	Med. Record, Sept. 1, 1883.
Lomer	77 "	Mult. Cyst.	Death.	Kelly and Sherwood, Johns Hop. Hosp. Reports, iii.
Samyrin	77 "	Cyst.	Recovery.	Amer. Journ. of Obst. and Diseases of Women and Children, Feb., 1884.
Borsini	77 "	Mult. Cyst.	Recovery.	Rev. Ital. di terap. ed. ig., Piacenzia, 1881, i, 367.
Staude	78 "	Mult. Cyst.	Recovery.	Kelly and Sherwood, Johns Hopkins Hosp. Reports, iii.
Heywood Smith	78 "	Mult. Cyst.	Recovery.	Lancet, 1892, ii.
Freund	78 "	Parovarian Cyst.	Recovery.	"Ovariotomie bei Greisinnen" Inaugural Dissertation, Strassburg, 1890.
Keith	78 or 80 "		Recovery.	Kelly and Sherwood, Johns Hopkins Hosp. Reports, iii.
Tuttle	79½ "	Mulf. Papill. Cyst.	Recovery.	Roosevelt Hosp. Records, N. Y., 1891.
Schroeder	79 "		Recovery.	Krankheiten d. Weibl. Geschl.
North	79 "	Cyst.	Recovery.	Brit. Med. Journ., 1903, ii, 1590.
Keith	79 "		Recovery.	Kelly and Sherwood, Johns Hopkins Hosp. Reports, iii.
Homans	79 "	Mult. Cyst.	Recovery.	Ibid.
Schroeder	80 "		Recovery.	Krankheiten d. Weibl. Geschl.
Richardson	80 "	Mult. Cyst.	Recovery.	Brit. Med. Journ., 1894.
Pippingsköld	80 "	Mult. Cyst.	Recovery.	Finska Läkare Handlinger, 1884, Helsingfors.
Owens	80 "	Parovarian Cyst.	Recovery.	Brit. Gynec. Journ., iv, 88.
Heywood Smith	81 "	Cyst.	Recovery.	Lancet, 1894, i, 1618.
Edis	81 "	Mult. Cyst.	Recovery.	Brit. Gynec. Journ., Aug., 1892, p. 162.
Cartledge	81 "	Mult. Cyst.	Recovery.	Trans. Southern Surg. & Gynec. Ass'n, x, 153.
Spencer	82 "	Mult. Cyst.	Recovery.	Brit. Med. Journ., 1893, ii, 1271.
Homans	82 "	Mult. Cyst.	Recovery.	Boston Med. & Surg. Jorn., 1888, cxvii, 454.
Remfrey	83 "	Cyst.	Recovery.	Trans. Obst. Soc., Lond., xxxvii, 152.
Kraft	84 "		Recovery.	Hospitalsridende, Copenhagen.
Bush	84 "		Recovery.	Kelly and Sherwood, Johns Hopkins Hosp. Reports, iii.
†Owens	87 "	Cyst.	Recovery.	Lancet, 1895, i, 542.
‡Thornton	94 "		Recovery.	Trans. Obst. Soc., Lond., xxxvii, 152.

† Second operation, first performed in 80th year.

‡ Oldest case.

TABLE I.

GENERAL RESULTS.

70 YRS. AND OVER.			10 YRS. AND UNDER.	
130		Total number of cases.	60	
16 cases.	12.3%	Mortality.	14 cases.	22.4%
4 "	3.07%	Result not ascertained.	5 "	8.3%

TABLE II.

RESULTS IN THE VARIOUS TUMORS.

70 YRS. AND OVER.				10 YRS. AND UNDER.		
cases.	% occurrence	mortal.		cases.	% occur.	mortal.
2	1.5%	0. %	Dermoids	22	35.2%	22.7%
65	50. %	11. %	Mult. Cysts	6	9.6%	16.6%
1	0.7%	100. %	Sarcoma	14	22.4%	35.7%
24	18. %	8.7%	Uniloc. Cysts	13	20.8%	23. %
9	6.9%	0. %	Papillomatous	3	4.8%	33.3%
4	3. %	75. %	Carcinoma	3	4.8%	33.3%
4	3. %	0. %	Fibroma	..	..	..
4	3. %	50. %	Parovarian	..	..	..
1	0.7%	0. %	Tuberculosis	..	..	..
..	..	..	Teratoma	1	1.6%	0. %
22	16.5%	4.5%	Unclassified	..	..	..

TABLE III.

CASES 80 YEARS OF AGE AND OVER.

Number of cases	14
Nature of Tumor	as far as ascertainable, all benign cysts.
Mortality	0%.

TABLE IV.

CASES 5 YEARS OF AGE AND UNDER.

Total number	24		
Deaths	8	Proportion of	33.3%
Results not given	2	" "	8.3%

TUMOR.	NUMBER OF CASES.	PROPORTION.	MORTALITY.
Dermoid	7	29.1%	65.1%
Sarcoma	7	29.1%	42.8%
Mult. Cyst	2	8.3%	50. %
Uniloc. Cyst	6	24.9%	16.6%
Papilloma	1	4.1%	0. %
Teratoma	1	4.1%	0. %

TABLE V.

CASES 5-10 YEARS OF AGE.

Total number of cases	36		
Mortality	6	Proportion of	16.3%
Results not given	3	" "	8.3%

TUMOR.	NUMBER OF CASES.	PROPORTION.	MORTALITY.
Dermoid	14	42.7%	7.8%
Sarcoma	8	24.4%	25. %
Cyst	6	16.3%	33.3%
Mult. Cyst	5	15.2%	0. %
Carcinoma	3	8.2%	33.3%
Papilloma	2	6.1%	50. %

TABLE VI.

Cases Arranged According to Year of Life.

AGE.	NUMBER OF CASES.	AGE.	NUMBER OF CASES.
Under 1 year...	2	70	35
1 ...	2	71	11
2 ...	7	72	14
3 ...	3	73	17
4 ...	7	74	11
5 ...	3	75	5
6 ...	1	76	5
7 ...	12	77	9
8 ...	8	78	4
9 ...	7	79	5
10 ...	8	80	4
.. ...	..	81	3
.. ...	..	82	2
.. ...	..	83	1
.. ...	..	84	2
.. ...	..	87	1
.. ...	..	94	1

History of the Case.

Elizabeth T., a girl aged 5, was admitted to the Johns Hopkins Genito-Urinary Dispensary on October 8, 1904.

Her *complaint* was that she was suffering from a vaginal discharge.

There was nothing of any importance in the family history, and except for two things her own past history was not interesting. The one was an attack of typhoid (?) in the first year of her life, and the other was a trauma, viz., a fall from a second-story window when she was 1½ years old.

The present illness on close questioning really dated from that fall. The child was apparently unhurt immediately after and went on with her playing as usual. Soon, however, she complained of *pain* which was so severe as to prevent sleep, and at times she would roll on the floor on her stomach trying to get relief. Her mother thought for a while that the child was shamming and acting as so many children do, for she could find nothing on feeling and looking at the child's abdomen which suggested to her anything wrong. This pain continued for a long time, about 1½ years, the mother thinks, and then subsided, except for occasional appearance. The next symptom was *swelling*, and this appeared only two months before visit to the dispensary. Following this there came *vaginal discharge*, for which the patient was brought here for relief.

On examination at the dispensary an offensive, white discharge was noted which the patient said was irritating. Other than some excoriation of the labia, there was no abnormality seen about the external genitalia.

Her second visit to the dispensary, on October 23, 1904, showed a change. The patient complained that the discharge which was formerly white had become pinkish, and the mother expressed some alarm. The genitalia were examined, and though no discharge was found there, in the garment there was every evidence of a bloody discharge. This led to further examination, and then there was found the tumor, which on the dispensary card is described as follows: "Above the pubic region there is a hard, rounded mass extending to the umbilicus, in shape, position as well as consistency resembling the uterus." Axillary and cervical glands were enlarged as well as the inguinal, and both mammæ were very large for a child of that age.

Having in mind the possibility of tumors in that region being distended bladder, Dr. Pollack and myself catheterized the patient but only 20 cc. of dark, clear straw-colored urine were obtained, and the tumor remained as before. Ether examination was not made then owing to lack of facilities for anæsthesia.

The patient was sent into the hospital where she was admitted on October 28, 1904. The results of examination there are these:

"Patient well nourished, no glands felt. *Chest* well formed. Breasts large for the age. Respiratory sounds well heard. A few fine râles in right axilla heard regularly at the end of inspiration, otherwise lungs clear. *Heart* P. M. I. in 4th interspace inside the mammary line. Sounds normal at apex and base. Pulse regular, 27 to ¼, of good volume.

"Hepatic dulness extends to costal margin. Edge of liver not felt. *Abdomen* looks rather full, especially just below the level of and at the side of the umbilicus. Appears symmetrical. On palpation the most prominent area of the abdomen is occupied by a more or less rounded, solid feeling mass, sharply circumscribed. Upper border of the tumor mass is about at the level of the umbilicus, but seems to pass a little higher up on the left side than on the right. Lower border crosses the median line about 2 fingers' breadths above the symphisis. More of the mass seems to be on the left side of the navel than on the right. Tumor the size of a large cocoanut, fairly freely movable and apparently not adherent to the pelvic organs of either side. Over the mass percussion is dull except along the left border where there is slight tympani. Neither kidneys nor spleen palpable. Pubic hairs well developed."

Measurements of Abdomen.

Girth at umbilicus	51.5	cm.
Greatest circumference	52.5	"
Distance from symphisis to umbilicus	13.5	"
" " umbilicus to xiphoid	13.5	"
" " " to right ant. sup. spine	10.5	"
" " " " left " " "	11.	"

Under chloroform anæsthesia, a combined vaginal and rectal examination showed a small uterus in anteflexion and that the mass was probably ovarian. A *diagnosis* of multilocular ovarian cyst was made by Dr. Kelly.

Before proceeding to tell of the operation and results, I should like to emphasize the sequence of the cardinal symptoms in this case. It is this:

Trauma, 3½ years before admission.

Pain, 3½ years before admission and not so severe recently.

Swelling, 2 months before admission.

White discharge, 3 to 4 weeks before admission.

Bloody discharge, 8 days before admission to hospital.

The *operation* performed by Dr. Kelly was a left Salpingo-oöphorectomy. A median incision was made and through this there was delivered a tumor of the left ovary about the size of a large cocoanut and freely movable. With it the left tube was removed, all of which was accompanied by no hæmorrhage. The right ovary which was seen, was small and apparently normal. The uterus was infantile, but rather larger than would be expected for 5 years. No evidence of metastasis of the tumor to the peritoneum or elsewhere. Catgut was alone employed, and the abdomen was closed in layers.

The patient stood the chloroform well and was removed to the ward in good condition, where she made an uneventful recovery and left the hospital, well, November 19.

Gross Appearance of the Tumor.—This tumor of the left ovary is ovoid in shape, and represents the whole organ tumified. It is 12.5 cm. long, 8.5 cm. broad, 7 cm. thick. Immediately after operation it had a somewhat boggy feel, something like that a soft solid tumor would give, but more suggesting a cyst with thick walls. It was mostly of a bluish-green tinge and shimmering, but in places could be seen beefy, brownish-looking areas showing through the glistening surface.

The tube is entirely attached to the tumor by a fold of peritoneum and this peritoneum extends along the tumor as far as ascertainable, about 5 cm., where it seems to affect a junction with a capsule about ¾ mm. thick. Radiating from the attachment of the tube are beefy-looking nodular yellowish-brown areas, extending all the way from 3 to 8 cm. On the surface these show a rich vascular supply.

Cutting the tumor in its long axis we find a capsule, ¾ mm. thick, from which extend bands of connective tissue which in some places more than others separate the underlying tissue into distinct alveoli, grayish in appearance and granular. The tissue underneath the capsule is found nothing other than the thick walls of a large cyst, the long axis of which corresponds with that of the tumified ovary. This wall varies from 2 to 4.5 cm. in thickness, and is for the most part alveoloid in arrangement, as heretofore described, though in some places there are more homogeneous white areas. The vascularity seems fair.

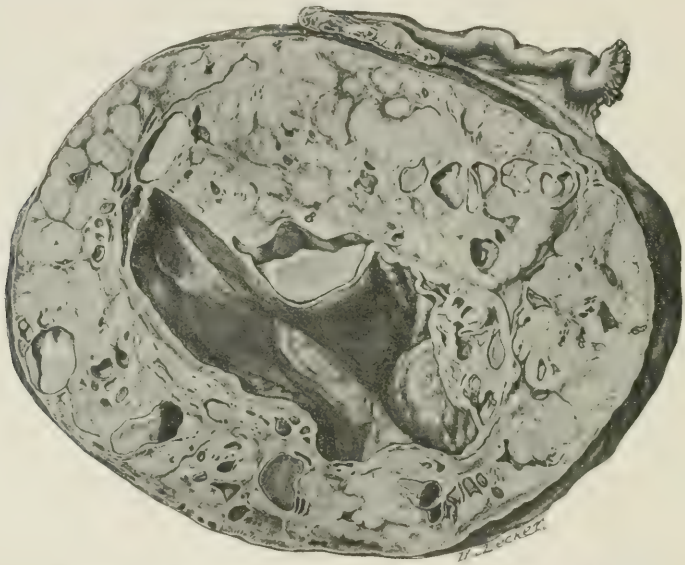
The large cyst is 7 cm. long, 4 cm. wide, 5 cm. through. It has a distinct lining membrane, thicker than the external capsule. This membrane is in some places perfectly smooth and arranged like a dome; in others it is thrown into rugæ and folds. The membrane is protruded in three distinct places by small underlying cysts, and at the external inferior angle of the cyst there protrudes a tumor 2 x 1 cm., apparently another cyst with a thick wall. Alongside of one of the cysts underneath the membrane of the large cyst, runs a good-sized vessel about ½ mm. in diameter.

In the walls of the large cyst, these walls making up most of the tumor, are 5 to 6 other cysts of less dimension, about 1.5 cm. in diameter, which contain a white gelatinous substance. Throughout the tumor are numerous small cysts of various sizes, each lined by a definite membrane.

Microscopic.—The diagnosis of adeno-carcinoma of the ovary was definitely made by Drs. Cullen and Hurdon. This was not done, however, until a very careful examination of many sections was undertaken. In some places the cellular arrangement of the new growth was highly suggestive of sarcoma and under a high magnification there was nothing to contraindicate that diagnosis. No alveolar arrangement was to be seen and the cells themselves were so aberrant as to suggest either the connective tissue or the epithelial tumor. At the advancing edges of the growth, however, a definite alveoloid and glandular arrangement was to be distinguished, and here the cells resembled much more suggestively the epithelial type.

Vascularity was good throughout and only in few places were there to be seen areas of slight degeneration and necrosis. Scattered throughout the sections were smaller cysts, the walls of which were plainly made out to be composed of many layered actively proliferating epithelium. Some of the cysts seemed to have as their content epithelial debris, others mucinous matter, and still others blood.

Trabeculæ of fibrous tissue were seen extending in from the capsule, but on the whole, stroma was present in not great proportion.



Gross Appearance of Longitudinal Section of the Tumefied Ovary with Adherent Tube.

This is the type of adeno-carcinoma of the ovary which Dr. Cullen describes as being extremely deceptive unless we examine many sections from various regions of the growth. It will usually be found, however, that at the advancing edges the carcinomatous arrangement will be quite typical and establish the diagnosis.

It is quite possible that some of the cases in literature diagnosed as sarcoma were rather tumors of this type.

As to the prognosis, it is certainly difficult to be of a definite frame of mind. Carcinoma occurs rarely in young children, at least in the ovary, and this is but the fourth case which has been operated on for removal of the growth. In the other three, Stolypinski's case is reported without giving the result, Gussenbauer's was well 6 months after the operation, and Leopold's died in 6 months from metastasis.

This tumor, though malignant, was extremely localized and even encapsulated. There were absolutely no signs of involvement of anything but the ovary and tube, and the operation was most successful in removing all of the morbid process. At the date of this writing, 3 months after the operation, the child is entirely well and active and shows no signs of any ailment.

From a consideration of the statistical study the following conclusions seemed justified:

First, and most important.—Age is no contraindication to operation in these cases.

Second.—Prognosis is extremely favorable in the aged, even in the most aged. In the young it is not so favorable, but nevertheless good.

Third.—Malignant ovarian tumors are rare in the aged but more common in the young, this greater frequency accounting for the greater mortality. The most frequent ovarian tumors in the aged are the benign cysts, particularly the multilocular variety, these tumors being comparatively rare in the young. Ovarian dermoids and sarcomata are the most frequent ovarian tumors in the young and the rarest in the aged.

In conclusion I must express my most sincere thanks to Dr. Kelly for the privilege of undertaking and reporting this work, and to Drs. Cullen, Hurdon and Holden for many points in pathology.

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The bibliography here appended includes only references to general considerations of the subject. The bibliography of the cases is found in the tables.

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Discussion.

Dr. Kelly.—This subject is most interesting on account of the tender age of the patients. Enough attention has not been paid to the examination of children gynæcologically, for we find practically nothing relating to this important subject in the average text-book and but little in the literature.

It is so easy to use a little chloroform in the child and the danger is so much less in children than with adults that we ought to make more frequent use of anæsthesia in examining them.

An important point is the relatively greater length of the examining finger. If the child's pelvis is half the size of the adult's, the finger is then twice as long in proportion. It reaches further into the abdomen and we can examine a much wider territory.

Another important point in the vaginal examination of children is that instead of using the finger, which produces trauma and is painful and always repulsive, you can use a little cylindrical speculum, from 10 to 15 mm. in diameter; put the child in the knee-chest position and place a pledget of cotton saturated with 10 per cent cocaine within the hymen and then after about 7 minutes introduce the speculum, and with the head-light you can investigate all parts of the vagina, which is distended, and the cervix, and you can at the same time take some of the secretions for microscopical examination. You can also better treat these patients in this way, making strong applications, if need be, to different areas. It does not hurt the child. They get used to the position and submit readily to treatment in this way.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Monday Evening, October 17, 1904.

The meeting was called to order at 8 o'clock by the President, Dr. Thomas B. Futcher.

Election of officers.—The Society elected Dr. J. C. Bloodgood, President and Dr. C. H. Bunting, Secretary for the ensuing year.

Loss of Entire Lower Lip. Repair by Flap from the Arm. Dr. Watts.

This boy, who is 15 years of age, was admitted to the service of Dr. Halsted on July 6, 1904, with the history of having had his lower lip bitten off two days before by a circus pony with which he was playing.

On examination, the entire lower lip was found to be absent, even the periosteum of the lower jaw having been stripped off in places. The wound was clean and free from infection.

Considering the great extent of the wound, it was thought best to cover the defect with a flap from the arm, rather than to attempt to obtain a flap from the face or neck. Accordingly a large flap was dissected from the right upper arm. This flap which included skin and subcutaneous fat was about 12 cm. in width and 18 cm. in length. Its under surface and the raw surface of the arm, from which it was taken, were covered with grafts removed from the thighs. All of these

grafts took well and at the end of ten days we had a flap with skin upon both sides. Some of the skin upon its under surface was intended to form a substitute for mucous membrane upon the unattached portion of the lip, and to some extent prevent subsequent contracture.

The patient had a bad bronchitis for some time, following this operation, and further operative procedure was thus postponed more than a month. During this delay, the flap, which had already become considerably shortened by the sloughing of its distal extremity due to imperfect circulation, contracted to a wonderful extent.

On August 18, we dissected up the flap somewhat farther, in order to lengthen it as much as possible, and then sutured its free extremity to the left side of the wound in the lip. A small portion of the vermilion border which had been preserved on this side, was sutured along the upper edge of the flap.

The arm was held in place by means of a plaster cast for a period of about three weeks. The flap was then severed from the arm. This was done under local anæsthesia in several stages to allow the circulation to become more perfectly established.

The patient seemed very comfortable in the cast, the strained position of the arm causing almost no pain. At two subsequent operations, at intervals of two or three weeks, the lower and right borders of the flap were trimmed up and sutured in position. A very good functional and cosmetic result was thus obtained.

The photographs show very clearly the various stages of the operation.

Report of Cases. Dr. Cullen.

Adeno-carcinoma of the Umbilicus.

Dr. Cullen exhibited a growth which he had recently removed from the region of the umbilicus. The inguinal glands had become enlarged in consequence of metastases from the original tumor. A pathological examination showed the growth to be an adeno-carcinoma with the typical glandular arrangement. There was no evidence of any malignant process in the peritoneum or in any of the abdominal organs.

Cancer of Liver.

About a year ago Dr. Cullen presented to the Society a specimen of carcinoma of the kidney which had been removed by an operation in January, 1903. The patient remained well until June, 1904, a period of 17 months, when she developed a tumor which increased rapidly in size. As her temperature was 102½° and she was losing weight rapidly, she was removed to a hospital and an immediate exploratory operation was advised, notwithstanding the fact that she had but a single cystic kidney. Upon the abdomen being opened a large cancerous nodule the size of a cocoanut was found in the liver. It was thought not to be a metastasis from the original tumor, as the stump had been found free from thickening or secondary nodules. At first an attempt was made to remove the nodule by means of the cautery, and although it was possible to roll the liver out of the abdomen, it was found impracticable to use it. Long blunt needles were accordingly forced through the liver substance and mattress sutures were introduced and the tissue afterwards was carefully separated by the knife, the tumor being kept constantly in a state of tension. Two or three sutures were introduced at a time and the dissection was progressively done. If a large vessel was encountered it was picked up and tied. By proceeding in this manner the operation was completed without the loss of more than two drams of blood and the patient was removed from the table with a pulse of 104. The upper and under surfaces of the liver were drained and the patient was able to leave the hospital in about four weeks. In September she was seen again and definite nodules had appeared on the left side. Of course any further operation is not to be thought of.

A certain Russian who has worked with Mikulicz has shown that operations upon the liver are feasible if suitable suture material and needles are employed. The needles are to be carefully forced through the liver, shoving the vessels aside in their passage, and as many sutures can be inserted as are needed. Sections of the carcinoma of the liver and also of the kidney show that the two growths are identical and lead to the conviction that the liver growth is secondary to that of the liver.

Melanotic Sarcoma with Metastases.

He also reported a case of a patient who had a pigmented mole of the neck which was associated with a similar condition in the peritoneal cavity.

Discussion.

Dr. Futcher.—I think the first of Dr. Cullen's cases should be emphasized, as showing the important part played by pigmented moles of the skin. Here was a patient who had a pigmented mole on the neck with metastases in the peritoneal cavity. The importance of these apparently benign tumors of the skin has recently been emphasized by Dr. Keen in a paper read before the Surgical Section of the American Medical Association, at Atlantic City, in which he recommends the removal of all pigmented moles, owing to their liability to become malignant and to cause the development of metastases in various parts of the body. Some of the members of the present house staff will probably recall a case shown in the dispensary clinic, two years ago, of a colored man who had a pigmented mole over the right scapular region, with enlarged glands in the right axilla. We happened to discover the existence of this mole and mentioned its probable association with the enlarged glands. The patient went to another hospital later, was operated upon, and the enlarged glands in the axilla proved to be a melanotic sarcoma, from which the patient eventually died.

The umbilical nodule which was present in Dr. Cullen's second case is also of interest, because one has to remember that metastases not infrequently occur in this situation in association with malignant disease of the liver and stomach.

Clinically, it is not so very uncommon to find these metastatic nodules at the umbilicus in malignant diseases of the deeper structures.

Recurring Phlebitis of Obscure Origin. Dr. Briggs.

(To appear later.)

Discussion.

Dr. B. B. Browne, Jr.—I should like to ask Dr. Briggs if there was any tendency to urticaria in his cases. He has investigated carefully the histories as to rheumatism and gout, but does not mention urticaria. We know that urticaria is most frequently met with in rheumatic and gouty subjects and it may possibly be at times a factor of considerable importance in inaugurating changes in the arteries and veins. That a sub-endothelial infiltration can occur in the arteries in urticaria, similar to the infiltration of serum under the rete of the skin forming the "wheels," I feel sure of, from a case of urticaria which I recently observed, in which a distinct systolic murmur and thrill were noted over the aortic area and the thrill could be felt in some of the larger vessels, indicating a temporary narrowing of the vessels. If this condition should occur in veins where the *vis a tergo* is slight we would have a factor for the condition Dr. Briggs speaks of. I think all cases of arterio-sclerosis and phlebitis should be investigated as to a previous history of urticaria, and a trial made to ascertain the presence or absence of "factitious urticaria."

Dr. Briggs.—I should perhaps like to add something in regard to the frequency with which the diagnosis of gout is made in these conditions. Tuckwell, who with Paget, has his name associated with the subject, laid it down as a law that every apparently spontaneous phlebitis was due to gout. He made spontaneous phlebitis as diagnostic of gout as Dr. Osler makes the recognition of tophi. To those who follow Tuckwell this present paper would have no justification, as all these cases would be characterized as gouty, but I have had unusually good opportunities of studying the first case and can exclude anything in the nature of gout. In the one other case that I have seen myself there was at the time I saw it Raynaud's Disease, and that has been put down in the list of ills which go with uric-acidæmia.

I should like to hear from Dr. MacCallum as to whether the pathological anlage is a condition of sclerosis or not. My idea was that a thrombus beginning at a sclerotic patch might extend beyond it itself, increase the sclerotic change, and so go on step by step up the vein. That is very tentative, of course, but there have been no studies at all made as to the pathology.

In regard to Dr. Browne's question, I would say again, with Dr. MacCallum, that my own views of the possible pathology were very theoretical and I have not studied the question as Dr. Browne has brought it up. There was no urticaria in the cases I saw, and in none of the other histories was it noted. There has been no mention made of that or of any other skin lesion.

Demonstration of Pathological Specimens. Dr. MacCallum.

The first case illustrates a condition seldom so clearly shown as in the present instance, the embolic occlusion of the coronary artery of the heart. The case was that of a man past middle age who had long shown evidences of the presence of a ventral endocarditis. The final illness which led to his death was remarkable for its duration, as the intense symptoms began in February and lasted until October without, however, being characterized by the sweats which are so frequent in the cases of ulcerative endocarditis of shorter duration. Death occurred quite suddenly and at the autopsy which was performed next day the following condition was found: The heart is somewhat enlarged. The right side of the heart is unaffected except for the presence of two or three fresh vegetations on the edges of the tricuspid valves. The left auricle, however, shows a rough nodular mass of fresh vegetations upon its posterior wall. The mitral valves are thickly covered with large soft vegetations which have apparently developed upon valves already the seat of old lesions. These vegetations extend over the chordæ tendineæ many of which are ruptured and their ends rounded off by the masses of vegetations. So extensive has this rupture of the chordæ tendineæ been that the valve flaps freely through the auriculo-ventricular orifice and at the autopsy its two leaflets were found projecting upward into the auricle. It seems probable that the vegetations upon the auricular wall may have resulted from the implantation of bacteria from these flapping valves. The aortic valves bear upon the central point of each segment bulky vegetations. Of special interest however, is the condition of the coronary arteries. The right one is open throughout, and its walls are smooth. The left is plugged at its orifice as with a cork by a thrombus mass which projects less than 1 cm. into its lumen and which hangs free in the sinus of Valsalva. This mass is fairly tightly wedged into the orifice but can be easily pulled out showing that it has no attachment to the vessel wall which is quite smooth at its points of lodgment. Further along in the course of the vessel which contained only fluid blood, there are some yellow patches, but the degree of sclerosis is nowhere very marked. From the position and relations of the plug and especially from the fact that it projects free into the sinus of Valsalva without any attachment to the adjacent valve or to the aortic wall and is not surrounded by clot, it seems certain that it is an embolic plug and the immediate cause of the man's death. The heart muscle shows no special alteration. There were numerous infarctions of varying age in spleen and kidneys. The case is chiefly of interest because of those reported in the literature there are so few in which the occlusion of the artery can be so certainly described as due to embolism and not to local thrombosis of the sclerotic vessel. Chiari, Oestreich, Barth and Hektoen report such cases while Marie denies the existence of coronary embolism.

To illustrate this case other specimens may be shown in which the coronary occlusion was shown and death did not result instantaneously. In these we cannot say definitely that the plugging was of embolic nature. In the first three

in which the sclerotic coronary arteries are occluded by thrombus masses throughout a considerable part of their course, definite sharply outlined anæmic infarctions of the heart wall have occurred, in one instance leading to such softening of the tissue that a sort of aneurysm of the heart wall has been produced. The pericardial surface of such infarctions is covered with a fibrinous deposit. Another specimen shows a practically complete occlusion of the coronary by arteriosclerotic patches in its walls with the result that not an infarct, but a gradual disintegration and disappearance of the heart muscle fibers has occurred throughout the area supplied by that artery leaving a thin fibrous scar-like wall over a considerable portion of the ventricle upon the inner surface of which large globular thrombi have formed.

The second case which I wish to bring before you is that of a man who had suffered for years from dysentery. Toward the termination of his life, perforation of the intestine had occurred in the neighborhood of the urinary bladder and an abscess formed which had eventually ruptured into the bladder—other abscess cavities or sinuses had extended from this point far through the pelvic tissues encircling and isolating even the symphysis pubis and the neck of the left femur.

At autopsy the bladder wall was found to present numerous papilliform projections over almost its whole surface, but especially large and abundant immediately about the orifice through which the intestinal contents could filter into the bladder. These seem quite superficial and microscopically prove to consist of a much inflamed fibrous stroma covered by a somewhat thickened and folded layer of epithelium.

The condition found in the large intestine is especially interesting in affording the obvious explanation of many cases of polyposis of the intestine, resulting from long-standing inflammatory processes. There are extensive ulcers which have destroyed the mucosa and part of the submucosa leaving only islands and bridges of mucosa. In the upper part of the intestine these are overgrown by fresh epithelium, in the lower part especially in the rectum they are still uncovered and the undermining is relatively recent. So that the islands and bridges of mucosa retain practically the appearance of normal mucosa. Higher up, however, the islands have been elevated and rounded off by the contraction of scar tissue about them—a similar rounding off of the bridges of mucosa has occurred and frequently they have been broken through at one end so as to hang free by the other end in the cavity of the intestine. The proliferation of the mucosa which remains in these tags soon converts them into bulkier masses which are the polypoid structures so frequently seen after ulceration processes from whatever cause. Naturally this cannot be offered as the explanation for the other and more regular forms of polypoid growths in the intestine which are of quite different nature.

November 7, 1904.

The meeting was called to order at 8:30 p. m., by the President, Dr. Joseph C. Bloodgood.

Biliary Cirrhosis of Family Type. Dr. Osler.

Cirrhosis of the liver is not an easy disease for students to understand, as the multiplicity of forms is confusing and the striking differences between the descriptions in the text-books and the clinical pictures in the ward upset the equanimity even of the third year student.

A very easy thing to remember, and perhaps the best practical division of the forms, is according to the tissues in which the disease begins, namely: portal cirrhosis, biliary cirrhosis and capsular cirrhosis. The portal form starts in the portal vessels, perilobular and sublobular; the biliary form begins in the small biliary vessels, the canaliculi inside the lobules; and the capsular form starts about the capsule of the liver. There is a great deal of dispute about the biliary type. Many English authorities refuse to recognize such a form. Yet I think there can be no doubt that such does exist, characterized by; first, a protracted course, extending over a period of from five to ten, or twelve years; secondly, a persistent jaundice, often of great intensity, always chronic (not as in the ordinary types of cirrhosis appearing and disappearing, but remaining as a prominent feature of the disease) and being generally very intense; thirdly, pains, which are often of a mild character, chiefly in the hepatic region; fourthly, its occurrence in comparatively young persons not subjects of alcoholism but coming in the third decade, or even earlier; it is the type met with in children; fifthly, the absence of all signs of portal obstruction, no ascites, no distended veins, no hæmorrhoids, or vomiting of blood; and lastly the frequency with which these patients have hæmorrhages, particularly from the skin and mucous membranes. There are some other minor points, but those are the most important. It differs most markedly from the ordinary alcoholic form in the occurrence in young persons, without an alcoholic history and the persistence of the jaundice over a period of years. On examination you find an enlarged and hard liver, usually too, enlargement of the spleen. Now I find that students, as soon as they find an enlarged liver regard it at once as a type of biliary cirrhosis. That is an error. All forms of hypertrophic cirrhosis are not this type. It may be an alcoholic; in the early stages of portal cirrhosis there is enlargement. There may also be enlargement due to the presence of fat. It is probably a special form of alcoholic cirrhosis with hypertrophy, in which the increase in bulk is due to the presence of large amounts of fat. It is possible in some cases that a remarkable regenerative process may produce hypertrophy; the great enlargement that we sometimes see in the left lobe of the liver in cirrhosis may be due to active regenerative changes.

We have had a few cases of the genuine type of biliary cirrhosis in the Hospital; only six or seven. Recently a case has brought to mind two remarkable instances of the disease that we studied in the session of 1898. They were brothers called W., one thirty-two, the other twenty-four years of age. They came of a healthy family; no alcoholic history. One had had jaundice for nearly eight years; the other for four years. As some of you will recall they were very much alike. Both came at intervals to the dispensary and the one who

subsequently came into the Hospital was watched by many of us with great interest. He had in addition to the persistent jaundice an enlarged liver, pains in the hepatic region, which recurred at intervals for many years, and the fourth especial feature was hæmorrhage. He had recurring attacks of bleeding from the nose and subsequently from the gums; he bled continuously from the gums during the last five years of his life, being almost never without a slight oozing from the gums. He died, as nearly all these cases do, of a terminal infection. He had an increase of the jaundice, high fever and delirium and in fact all the features of an acute toxæmia. Blood cultures were made and the staphylococcus and streptococcus isolated. He had a greatly enlarged liver and a moderately enlarged spleen.

The brother had jaundice for four years and was intensely yellow. He too had pains on the right side in the region of the liver and had hæmorrhages, chiefly epistaxis. He also died of an acute terminal infection with high fever. There was no autopsy in his case.

Recently there has been in the wards a case that comes under this family variety or form of cirrhosis. A man, twenty-three years of age, a farmer from Virginia. He was admitted ten days or two weeks ago and had a good family history, so far as his father and mother and grand parents were concerned. He had had measles at ten and diphtheria and pneumonia six or seven years ago. He had had no malaria, no lues, and had no alcoholic history. He had had a chronic otitis media for several years. He had had an attack of jaundice at the fifth year from which he recovered. In October, '99, five years ago, he first noticed this yellow color, which has never cleared up, though it became lighter at times. He has lost in weight nearly twenty pounds in the past few months. He has occasionally had epistaxis and several times has vomited a small quantity of blood. He has had no pain and no fever. The coagulation time was three minutes. The liver was felt below the costal border and did not seem greatly enlarged; but the post mortem showed it to be much larger than we supposed from our palpation. There was no leucocytosis. The man's life was very miserable; he was in a wretched condition, and was anxious for operation. He was brought down one day for operation, but his blood coagulation time had gone up to ten or twelve minutes and he was sent back. On the day he was operated upon his coagulation time was one minute and forty-five seconds. At operation the bile passages were found clear, there was no obstruction. He had a few gall stones in the gall-bladder, but there was nothing in the bile passages themselves. He bled as these cases so often do following operation and died directly of the hæmorrhage. The post mortem Dr. MacCallum will speak of. We found out from a brother after the death, that this jaundice from which he had suffered was a family condition. He had two brothers with jaundice and two sisters. One brother had been operated upon in Washington Territory and the brother who came had jaundice and had had it for five years. Two sisters also have jaundice, so that it is quite possible that this represents another illustration of the family form of this type of cirrhosis. The condition of the liver is interesting and it is quite possible that it is an early stage of this capillary angio-cholitis which is supposed to be the essential anatomical feature in the biliary or true hypertrophic cirrhosis.

Discussion.

Dr. MacCallum.—At the autopsy it was found that the gall-bladder had been opened and drained—its wall was somewhat scarred, but especially thickened by the hæmorrhage which had occurred since the operation. The liver was very dark green in color, but the lobulation was not distorted, there were no evident bands of fibrous tissue throughout its substance and its consistence was not increased. The cystic duct, common duct, and hepatic ducts as far as they could be traced into the liver were delicate and normal in appearance. They showed no evidence of the presence of obstructions of any kind.

Microscopically it is seen that there is a very slight increase in the connective tissue about the portal spaces and in some instances about the central veins, but this is so slight as to be hardly distinguishable except by the aid of some special stain.

The liver cells in each lobule show a very marked degenerative change, especially in the more central portion of the lobule about the central vein. Many of them are actually necrotic and disintegrated. Leucocytes frequently crowd the capillaries and lie about among the broken cells in these areas. Where the bile capillaries are preserved they are frequently distended with green bile pigment.

There is no satisfactory explanation of the jaundice to be derived from this microscopical picture, although possibly the explanation recently offered by Eppinger for the development of icterus might apply here.

The process suggests a toxic origin, but it is difficult to decide as to the source of such a toxic substance.

Dr. Osler.—One interesting thing about these cases is that though intensely jaundiced, and perhaps in some of them a deeper jaundice than we see in any cases except those of malignant disease, it is not an obstructive jaundice because bile is present in the stools, though in small quantities. Even these cases of most intense jaundice still have bile in the stools. The whole essence of the process is apparently a capillary angio-cholitis. Of course in this case it may be an early stage of a process which may last for ten or more years.

Crossed Dissociated Sensory Paralysis with Lesion of Medulla. Dr. Thomas.

Situs Transversus and Atresia of the Pylorus. Clinical Notes, Dr. Little. Pathological Notes, Mr. H. F. Helmholz.

(To appear later.)

November 21, 1904.

The meeting was called to order at 8 P. M., by the President, Dr. Joseph C. Bloodgood.

Experimental Streptococcus Arthritis. DR. COLE.

I wish to speak briefly tonight of some work we have been doing in regard to arthritis induced by the action of streptococci, with especial reference to the etiology of acute articular rheumatism. At present acute articular rheumatism is regarded by most authorities as an acute infectious disease. Those who consider that it is due to bacteria hold various theories. These are that it is due to:

1. A specific micro-organism, as yet undiscovered.
2. Various pyogenetic cocci, mainly the ordinary streptococci; that it is a mild form of pyemia.
3. A specific streptococcus or diplococcus.
4. A specific bacillus—Bacillus of Achalme.

At present the second and third views have the most supporters and it is mainly these that we propose to consider.

The reason why this disease is thought to be due to a streptococcus or diplococcus is that in a number of cases clinically resembling acute articular rheumatism streptococci or diplococci have been isolated from the joints, from the heart's blood or from inflammatory exudates. Also Meyer, recognizing the frequent association of angina and rheumatism, made cultures from the throats of rheumatic patients suffering from angina and isolated from a number of them a streptococcus, which, when injected into animals, produced characteristic lesions or lesions resembling those of acute articular rheumatism. In 1902, Menzer reviewed the whole question and he concluded:

The cause of acute articular rheumatism is not a specific bacterium, but the ordinary parasites of the mouth, which under certain conditions have become pathogenic. Almost exclusively are streptococci the organisms concerned. These streptococci are by far the most common cause of the different forms of angina, and also of the so-called angina rheumatica.

Notwithstanding these conclusions regarding the specificity of these cocci, several English observers, namely, Poynton and Paine, Ainley Walker, Beaton and Walker, Shaw and Beattie, have continued to report the isolation of streptococci or diplococci from rheumatism cases, going so far as to name these Micrococcus or Diplococcus rheumaticus.

The claims of these observers as to the specificity of these organisms are based on cultural and morphological peculiarities and on experimental results obtained by the injection of these organisms into animals. As regards morphology, these observers are not unanimous, some of them considering the organism a streptococcus, others a diplococcus. Most agree, however, that they may appear either as streptococci or as diplococci, depending upon their environment. In fact, Walker, who has made the most extensive studies of the morphology and cultural characteristics of these organisms says:

We have no hesitation in saying that *without animal experiments it would almost certainly be diagnosed as an ordinary streptococcus by anyone* to whom cultures and stained preparations were submitted without comment.

Culturally this organism resembles a streptococcus, but that it is specifically different from the ordinary streptococci is rendered probable by our results on the application of the test of Marmorek.

Since, however, the value of this test for determining specificity has had so much doubt thrown upon it by the work of Meyer, and Aronson, and others, and especially since Walker's observations were so few and reported with such slight detail, this evidence at present, at least, cannot be considered very valuable.

The same may be said for the specific reaction claimed for it by Shaw, namely, the property of causing blood agar to change in color to a dull brown or rusty tint when this organism is grown upon it, while in the case of the common streptococcus this does not occur. Schottmüller, however, has shown that this property is common to a large number of streptococci from widely differing sources.

From all this it is evident that the claims for specificity of this organism must rest not on morphological or cultural grounds but on the peculiar lesions produced when inoculated into animals.

Practically all of the observers who have been mentioned as describing a coccus associated with rheumatic fever, have been able, by the inoculation into rabbits of quite large amounts of this streptococcus, to induce multiple arthritis of variable grades of intensity, in some cases endocarditis and pericarditis, and in a few experiments a condition said by the writers to resemble chorea.

My own work began with the study of a streptococcus isolated from the circulating blood of a man with endocarditis and septicæmia. For a year or more he had been troubled with "rheumatic pains in his joints," though no definite history of acute rheumatic fever could be obtained.

However, thinking it possible that the streptococcus might be the one described by Poynton and Payne, and others, we began inoculating rabbits, and rather to our surprise found that arthritis was produced with marked regularity, almost every rabbit showing some grade of arthritis. As, however, the cultures of this organism did not differ essentially from those of ordinary streptococci, we thought it better to proceed with streptococci from other sources. We made cultures and inoculations from six races of streptococci. The sources of these various races were: peritonitis following carcinoma of the stomach; puerperal fever-autopsy; blood during life in terminal septicæmia following myocarditis; empyema; blood during life in septicæmia following appendicitis; scarlet fever adenitis.

The diversity in the sources of these races renders it impossible that they could all have had any association with rheumatism, so that we could not have been working always with the so-called "Micrococcus rheumaticus."

The technique of inoculation was practically that of the English observers. The cocci were grown on solid media, an emulsion was then made and this was inoculated into the ear vein of a rabbit. With all seven races studied intravenous inoculation of amounts insufficient to cause death of the animals within six or seven days led to the production of mild grades of arthritis.

On about the fourth or fifth day after inoculation the rabbit usually appeared ill, remained quietly in a corner of its cage and only when it was put upon the floor and urged to move about would one see that it was quite lame. The lameness would sometimes appear in one leg and then in a day or two other joints would become involved. Usually recovery from the lameness occurred in a few days but in some death occurred. Other rabbits we killed while they were still lame. Still others we allowed to recover and then reinoculated when they would again show signs of arthritis. One we kept reinoculating in this way over a period of several months.

When the rabbits died or were killed, the joints were all carefully examined and certain of the joints were always found to contain a thick, sticky, tenacious exudate, very different from that found in the normal joints. In these affected joints the surface of the cartilage was smooth, but the capsular lining was usually injected and red and covered with the thick turbid exudate. There was also usually considerable œdema about the joint. Microscopical sections were made from most of the joints and the lesions carefully studied. Smears made from the exudate showed numerous polymorphonuclear leucocytes and a few mononuclear cells. Almost invariably diplococci were found in these smears; occasionally chains of three or four pairs were found. The cocci were usually flattened on one side, the flat sides approximated, so that one seeing them for the first time would certainly call them diplococci and not streptococci. Cultures were always made from the affected joints, however, and a typical growth of streptococci occurred in most cases.

In two of the rabbits a typical endocarditis occurred. The hearts of these rabbits have been preserved and I pass them around so that you can see the small vegetations present on the mitral valves.

Two of the animals on the day before death showed typical twitchings and incoordinate movements. They threw themselves about in the cage and when placed on the floor would run around and dash their heads into the wall, a condition which might be considered choreiform, but not at all analagous to the chorea we see in children.

The only reason we have to offer why this arthritis has not previously been noted by all observers who have done experimental work with streptococci is that usually such work is done with the idea of testing the pathogenicity of organisms, usually determined by the amount and time necessary to produce a fatal result, and when post-mortem examinations were made the joints have not been carefully studied as a routine procedure. During life a rabbit having arthritis will usually remain quiet in one corner of the cage, and it is only when the rabbit is placed on the open floor and urged to move about that the lameness is detected. So, too, in most cases the swelling of the joint, unless extreme, is rather difficult to detect through the thick skin and fur. Often a considerable distension of the joint and œdema of the surrounding tissues has been found after dissecting away the skin, when previously it could not with certainty be detected. In many cases the joint affection is mild, and unless one were especially interested in looking for it, it might be overlooked. It is only by making a routine examination of all joints that the lesions are discovered.

It may be stated that, while slight morphological and cultural differences existed between the various races of streptococci studied, none of these were constant enough to speak of a distinct variety. Each one differed slightly from the other in its manner of growth in bouillon, its growth in milk, etc. To make such comparative studies of any value, they should be repeated at intervals over a considerable length of time, to make certain that the characteristics have at least a fair degree of constancy. This has not yet been done with the organisms studied.

There was considerable variation in the pathogenicity as measured by the lethal dose of the races studied. Thus, while with certain of the organisms an emulsion made from the growth on six to eight tubes could be safely inoculated, in the case of the streptococcus obtained from the cervical adenitis in scarlet fever, one fourth of a tube caused death in five days when so inoculated.

As a result of this work we may say that arthritis and endocarditis may be produced by the intravenous inoculation of rabbits with streptococci from widely varying sources and that the results are similar to those described as produced by the inoculation with the so-called Micrococcus rheumaticus. I have seen the joints resulting from the inoculation of the organism isolated by Wassermann and also those produced by the organism isolated by Longcope and they do not differ from those produced here by these various streptococci.

Whether or not rheumatism is a form of streptococcus infection, I think we must still consider as undecided.

Discussion.

Dr. Cole.—During the past three years, in practically all cases of acute articular rheumatism treated in this Hospital, routine cultures have been made from the blood, and from the joints whenever any effusion was present in the latter. So far all our cultures from cases of acute articular rheumatism have been negative.

Similar results are reported by Philipp in the Deutsche Archiv für klinische Medicin, Band 76. He made cultures twenty-one times from the blood and six times from the joints in twenty-four cases of acute articular rheumatism. The cultures were made in a great variety of both solid and liquid media, and were cultivated both aërobically and anaërobically. Inoculations directly from patients were also made into guinea-pigs, rabbits, dogs, monkeys, and calves. But from none of these cases could any bacteria be cultivated.

Dr. Thayer.—That was the result obtained by Singer some years ago.

Professor Smith on the Jersey Mosquito. Dr. Kelly.

Prof. J. C. Smith, of Rutgers College, President of the Entomological Institute, who has written an admirable hand book on the mosquitoes of New Jersey, giving the

life habits of the more important species and an analytical key of some thirty species, presented me about a year ago with this handsome collection of eggs, embryos, larvæ and adult forms. Nothing like it, I believe, has ever been prepared before. There are as you see a great variety of culices, the anopheles punctipennis, and the psophora or giant mosquito. In each upper row, on the most delicate entomological pins, are the males, and on the lower, the females, while the bottles contain the larval forms.

I desire to present this to the Hospital, to be placed where it can be seen and studied by our students.

I would ask if there is any evidence that the anopheles punctipennis carries the malarial parasite? This whole question of mosquito distribution is so important that I will, with Dr. Osler's permission, offer to any member of the third year class, who presents next year a satisfactory thesis upon this subject, discussing the distribution of mosquitoes and presenting a map showing where they breed about the city, with suggestions as to the best methods of getting rid of them, a prize of fifty dollars.

December 5, 1904

Gastric Ulcer: Clinical Varieties and Symptoms. Dr. Howard.

Dr. Howard gave the results of a careful study of ulcer of the stomach and duodenum based upon a series of eighty-two cases, with the following conclusions:

1. Gastric ulcer is rare in the Johns Hopkins Hospital as compared with cancer, the respective incidences being 1 to 225 and 1 to 56 general admissions.

2. Gastric ulcer in our series was as common in the male as in the female. In the male the percentage of greatest frequency was between the ages of forty and fifty—a decade later than usual.

3. Ulcer was in our cases relatively more frequent in the colored race and among Germans.

4. Vomiting occurred in 85.3 per cent; pain in 82.9 per cent, and hæmatemesis in 75.6 per cent.

5. Great loss of weight may be present; thus, in 36 cases there was a loss of more than ten pounds, and in 9 of forty pounds or more.

6. Our statistics would indicate that hyperchlorhydria is not so constant as usually maintained; it was present in only 17.6 per cent of our cases.

7. The blood picture is one of chloranæmia as seen from the average count (hæmoglobin, 58 per cent; red blood corpuscles, 4,071,000; white blood corpuscles, 7500 per c. mm.

8. Hæmorrhage was the cause of death in 8.5 per cent of the total number of cases, and in 29.5 per cent of the fatal cases.

9. Perforation is rare (3 cases, or 3.6 per cent of our series). General peritonitis occurred in but one instance (1.2 per cent).

10. Ulcus carcinomatosum is rare—at least 4.8 per cent of our series.

11. Operation is indicated in all cases with perforation or perigastric adhesions, and in cases of copious or recurring hæmorrhage, when medical means have failed after a fair trial.

12. The mortality of the series was 29.3 per cent; in the cases, however, who received treatment there was a mortality of only 18.8 per cent; in those receiving medical treatment alone, 8.6 per cent.

Gastric Ulcer: Diagnosis and Medical Treatment. Dr. McCrae.

In common with the majority of diseases one must recognise that the diagnosis of gastric ulcer in typical cases is usually very easy, in atypical cases very difficult. We have to keep in mind that a large number of cases are latent and that it is sometimes impossible to make a diagnosis. The experience of the post mortem table proves that. Perforation or hæmorrhage may occur without any previous history. Concerning ordinary typical cases very little requires to be said. The pain with its characteristics, the presence of blood and especially of blood microscopically are important. In a large percentage of cases blood is vomited, but it is important in cases in which there is no vomiting of blood to make a careful microscopical examination. One has to exclude cases where the presence of blood follows excessive straining. Hyperacidity is not regarded by us in this country as so frequent as by the German authorities. Coming to the more atypical cases one has to distinguish certain other conditions from ulcer, the most frequent of which are the various gastric neuroses. That is in many cases difficult to do and in many instances one has to leave the matter open. Fortunately the medical treatment may be the same whether the case be one of neurosis or ulcer. The pain is not so constant in the neuroses and repeated gastric analysis usually aids the diagnosis. Next probably comes the diagnosis from gall-stones. The character of the gall-stone attacks with their very severe character, the rapid onset and rapid recovery, generally help us, and the symptoms are not so constant. The gastric crises of locomotor ataxia rarely give much difficulty. Practically all the acute abdominal conditions may give trouble at times. In the chronic ulcer the most important point in diagnosis is that to be made between ulcer and neoplasm, and in many cases this is very difficult. In the majority of cases the finding of a large mass and free hydrochloric acid speaks for ulcer, but we have to remember the possibility of a neoplasm having developed in a former ulcer, in which the free hydrochloric acid is retained. In such a case if one is in doubt there should be no hesitancy in turning the case over for surgical exploration, especially as the procedure for diagnosis and treatment is the same.

Turning to the question of treatment I think it is well to discuss this in three groups of cases; first, the doubtful cases, largely composed of those where the diagnosis is between gastric neurosis and ulcer. The treatment of this doubtful group may come under the same heading as in the second group, the ordinary acute ulcer, the third group being the chronic ulcer.

As to the treatment of the ordinary acute gastric ulcer, in

which one may also put the doubtful cases, the first essential is absolute rest in bed for a period of at least four weeks in the average cases. The rest is important in itself because by keeping the patient in bed you can control the question of feeding. In the majority of cases if the necessity of rest is properly explained, stress being laid upon the danger of the ulcer becoming chronic and the complications that may arise, the majority of patients will submit. In the treatment of the ulcer itself the essentials are rest, absence of irritation and the securing of the best blood supply. Rest is best secured in the majority of cases by the withdrawal of food by the mouth for a few days. That depends a little on the severity of the case and an average of four to six days is generally enough, during which time the patient is to be fed by the bowel. A small amount of water by the mouth may be allowed. As a rule at the end of four days of starvation it is well to begin with small amounts of liquid nourishment. Of foods milk stands first, probably given best peptonized or in the form of whey. One should begin with small quantities and gradually increase the amount. As a rule it is best for the first ten to fourteen days not to give anything else but milk. Probably a quart is enough in the majority of patients, though some writers advise two quarts a day. As a rule it should be given well diluted and with an alkali, either with an alkaline water or with a small amount of bicarbonate of soda. At the end of ten days or two weeks one may increase the diet gradually and more milk may be given, then the gruels, beef juice, jelly, etc., until at the end of four weeks one has the the patient back on soft food again. It pays to be conservative, to go slowly, increasing very little from day to day, and if any signs of irritation arise put the patient back on liquid diet at once.

To reduce the gastric secretions atropin may be given in 1/150 or 1/100 grain doses before food. Large quantities of alkalies should be given, sodium bicarbonate and magnesium carbonate in large doses. This probably in the majority of cases will be enough but there are a few other drugs which we usually employ, not perhaps in every case, with the idea of assisting the process of healing. Perhaps the most useful are bismuth, silver nitrate and olive oil. In giving bismuth in gastric ulcer one should give large doses, if by the mouth, dram doses at least four to six times in the twenty-four hours. An ounce may be given at one time through the stomach tube. Many writers advise washing out the stomach and then putting in an ounce of bismuth with water. Silver nitrate may be given in capsule, followed by half a glass of water, or dissolved and taken through the tube, the essential thing being to have it fresh. Of olive oil an ounce may be given at a time, perhaps four times in the twenty-four hours. A doubtful question is that of washing out the stomach. I think in the majority of cases one may wash out the stomach if the patient is having pain, lavage with an alkaline water often giving relief. In the majority of cases, however, the tube is not required. There is little danger if it is done with caution. An important point to keep in mind is that your treatment must not stop when the patient, so to speak, is well. The gastric ulcer is very prone to recur and one should certainly keep track of these patients for a year, watching the diet and keeping up the use of the alkalies. If this were done there would be fewer cases of relapse. The use of alkaline salines is always helpful, for instance, Carlsbad salts. If there be anæmia iron should be given.

In the chronic cases we have quite a different condition. The ordinary acute case if taken early and treated systematically does extremely well; in the chronic ulcer it is different. But in the majority of these cases, unless there is indication for operation, I think it is well to give the same treatment as in the acute cases, remembering that it must be for a much longer time. If they do not improve under the ordinary treatment which we have gone over it is well to consider the advisability of surgical measures, and I think they are certainly demanded in three conditions: one for diagnosis, where there is doubt as to malignancy. The second is in cases of repeated hæmorrhages. If you wait until the patient is exhausted and his hæmoglobin is low from repeated hæmorrhages you greatly handicap his chances. The third is the occurrence of pyloric stenosis due to ulcer.

With care in the diet and the use of the drugs mentioned pain is usually not troublesome, but in many cases certain of the sedatives are required. Small doses of the bromides with codein is enough sometimes but in some cases morphia must be given. It is best to give it by mouth and accompanied by bismuth. Morphia hypodermically is to be advised against in ulcer cases. There is only one treatment for perforation and that is immediate operation, but in order to be able to do that you must have made preparation beforehand. Just as the prognosis in operation for perforation in typhoid fever depends upon quick diagnosis, so it is in perforation of gastric ulcer. Those looking after the case should report at once any sudden abdominal pain or any sudden change in the patient's condition. The treatment of hæmorrhage in the acute case is largely that of rest; I am speaking of the ordinary hæmorrhage which we see and which is generally not alarming. Practically all we have to do is to cut off the food by mouth and give morphia hypodermically. The value of styptic drugs by the mouth is doubtful. There are certain of these cases in which hæmorrhage is the direct cause of death, and in such cases operative procedures may be justified. If there are repeated hæmorrhages it will be well to have the patient operated on. In the great majority of cases, as in cases of pulmonary hæmorrhages, if the patient does not die at once there is very little danger. In the chronic cases the repeated hæmorrhages are a strong indication for operation.

The patient with gastric ulcer has the right to demand two things: first, from the surgeon, that his technique be as good as possible so that there is no risk more than that incident to his condition in having operative procedures carried out, and I think the surgeons have fulfilled this; second, he has a right to ask the physician that he recognise when the necessity for surgical interference has come.

Discussion.

Dr. Pancoast.—I should like to report two or three unusual features in a case of perforation. The first is that although the perforation occurred forty-eight hours before operation the patient is alive at the end of three weeks. He had a high grade of peritonitis throughout the greater peritoneal cavity and so far as the general peritoneal cavity is concerned the peritoneum is taking care of itself. A second point of interest to me is that the patient was distinctly jaundiced and had bile in the urine, and in his general peritoneal cavity. There was a large amount of bile in the general peritoneal cavity, so much that the contents were dark green. A third point of interest is that he has developed since the first operation two secondary abscesses. One in the pelvis was easily drained through an incision on the other side of the abdomen. The other abscess was drained last night through the 9th intercostal space on the left side. 1600 cc. of pus were removed. It was probably a subphrenic abscess. The patient is very ill and probably will not recover.

December 19, 1904.

The President, Dr. Joseph C. Bloodgood, in the chair.

Report of a Case of Ulcerative Endocarditis, with Embolism of the Aorta. Dr. Osler.

The patient, aged 12 years, a factory girl, was admitted November 3, 1904. Past history negative. No history of genito-urinary infection. Onset of present illness October 24, with chill, fever, headache and some abdominal pain. Chill came on while at work and was followed by a chill every day afterward. She vomited daily and was thought to have typhoid fever. She was admitted to Ward G on November 3. Physical examination was practically negative, except for a rather rough systolic murmur at the apex transmitted outward to anterior axillary line, but not heard in the axilla. The second pulmonic sound was not accentuated. Edge of spleen could be felt. There was active knee-jerk and ankle clonus present. Koenig's sign absent. Leucocytes were 28,000. Temperature high, irregular, and there was a daily chill. Sweating slight. The systolic murmur increased in intensity and was transmitted into axilla. Petechiæ appeared over the face, chest and arms. On November 8, lumbar puncture gave 70 cc. very clear fluid. Pressure 280 mm. Culture negative. There was a slight vaginal discharge but no intracellular diplococci. On December 4, for the first time there was a presystolic thrill and rumble. She also cried out with pain in the lower limbs and there was apparently anæsthesia below the knees. Stools and urine were passed involuntarily. No pulsation could be felt in the dorsalis pedis or popliteal. On December 5, feet were not cold or discolored. Knee-jerks were present, but diminished. On December 7, pulsation felt faintly in popliteal. Widal was repeatedly negative. Blood cultures were made on November 4, November 11 and December 4. Urine cultures on December 15, and November 22. The patient died December 16.

The illness was of six weeks, with high and irregular fever, and with no special embolic features until two weeks before death; there was a great deal of doubt at first whether it was typhoid fever or endocarditis. The diagnosis was reached by exclusion, and it was not until the murmur increased in intensity and changed in character and the cardiac symptoms became more positive that a definite diagnosis was made of ulcerative endocarditis. A point of special interest is that a week before death she had paralysis of her legs with slight change in sensation and complete absence of pulsation in the arteries. Of course we suspected a plugging of the vessels, probably of the aorta, but strange to say, instead of the usual sequence, namely, change in color of the feet, at first bluish, then black, and almost certainly followed by gangrene, in this case the legs remained cold, sensation was reduced; there was no pulsation in the vessels, but no gangrene followed, and there was not even change in the color, a most unusual thing.

The specimen, which is a most remarkable one, shows typical ulcerative endocarditis of the mitral valve with a large thrombus occupying the lower part of the aorta and blocking it completely. There was a small embolus in the spleen and one in one kidney.

We had another illustration of plugging of the aorta by thrombus in a case of chronic mitral disease and I show the specimen.

Case of Typhoid Fever showing some Unusual Features. Dr. Cole.

Dr. Osler has asked me to speak of a case of typhoid fever in a young colored girl, showing some unusual features. The child, aged 10 years, was admitted on December 8. The onset of the illness occurred on December 1 with a violent attack of vomiting. Following this there was fever and some pain in the right side of the abdomen. There was no delirium. The child remained in bed, but on December 8 walked to the hospital and did not seem very ill. While waiting to be sent to the ward, however, there suddenly developed active, talkative delirium. This continued almost constantly, and slight stiffness of the neck and extremities developed. On December 12, a lumbar puncture was performed and 25 cc. of fluid obtained under normal pressure. No growth occurred in the cultures from this fluid and microscopical examination was negative. The Widal test performed on December 10 was also negative. The fever continued high, between 102° and 105°. The signs of meningitis became more definite, there was retraction of the head, the knee-jerks were active, and a fairly definite Kernig's sign was obtained.

Notwithstanding this, a second lumbar puncture performed on December 16 gave negative results as before. On the same day, however, the Widal test was positive, and in cultures made from the blood a pure growth of *B. typhosus* developed. The abdominal pain continued; she grew gradually worse and died on December 18.

This case was interesting, first, from the standpoint of diag-

nosis. The marked meningeal features and absence of any definite signs of typhoid fever made the diagnosis difficult. The first definite evidence that we were dealing with a case of typhoid fever was given by the blood cultures and Widal reaction. Second, this case well illustrates the not infrequent occurrence of marked meningeal features during typhoid fever. As I have previously stated, these cases may be divided into three groups: first, those in which there is no direct association of the bacilli with the cerebral manifestations, and no lesions are to be found in the brain to account for the symptoms; second, those in which the bacilli are present in the spinal fluid, but no marked inflammation of the meninges is present; and third, the cases of true suppurative typhoid meningitis.

This case is a good example of the first group, and of those cases to which certain of the French writers have applied the term *méningisme*. In this case lumbar puncture was performed on two occasions with negative results, and at autopsy absolutely no lesions could be demonstrated in the brain or meninges. Typical typhoidal lesions were found in the intestines and there was very marked enlargement of the lymphatic glands, the mesenteric glands and Peyer's patches being of enormous size, as you can see in these specimens which I exhibit.

Discussion.

Dr. Osler.—It is difficult in these cases to determine whether a true meningitis is present or not. I would refer you to Stokes' well-known dictum that the acute congestion of the cerebro-spinal centers in fever may give rise to all of the symptoms of a meningitis; there may be no single symptom absent in cases where there is only this extreme engorgement. We have had several instances where the meningeal symptoms were very marked without the existence of actual meningitis.

Puerperal Infection with Gas Bacillus. Dr. Little.

(To appear in April Bulletin.)

Report of a Case of Arteriovenous Aneurism of the Thigh. Dr. Osler.

Many of you may recall that about three weeks ago I showed at the clinic three remarkable cases of aneurism, one of them an arteriovenous aneurism of the femoral artery in a man aged twenty-nine years, who was shot 15 years ago. The tumor has gradually grown to about half the size of a pineapple. The leg was greatly enlarged, blue to the foot, and on palpation over the tumor there was a remarkable vibratory thrill which could be felt up the thigh over the entire anterior and posterior portion of the leg. On listening with the stethoscope one could hear a murmur of great intensity, a humming-top murmur, intensified with each systole. I called your attention at that time to the original description of the disease by William Hunter, which pass around again, as it is the first account of this form of aneurism. Yesterday this man died suddenly, and Drs. Cole and MacCallum secured the specimen.

Discussion.

Dr. MacCallum.—Orth divides the traumatic aneurisms in which communication between artery and vein is established into three groups: (1) the arteriovenous aneurism in which an ordinary aneurism has ruptured into a vein; (2) the aneurisma varicosum in which a sac lying between the two vessels forms the communication between them; and (3) the varico-aneurismaticus in which the artery and vein are intimately united and communicate through openings in their walls. The sac which forms in the second variety is the result of the encapsulation of a hæmatoma through which the blood still circulates.

Bramann (Arch. f. klin. Chir., XXXIII), has collected 141 cases, of which the greater number resulted from venesection, but there were also 35 cases of communication between the femoral artery and vein. The condition is usually produced by such an injury as a stab or gunshot wound. The present case does not correspond precisely with any of Orth's classes. The femoral artery is greatly dilated and at about the beginning of the lower third of the thigh it shows two perforations separated by a bridge of tissue. The femoral vein lying close beside it shows one perforation at the same level. A probe can be passed from the artery into the vein through these apertures; in so doing it passes the orifice or mouth of a sac about 12 cm. in diameter which lies to the inner side and somewhat in front of the artery and vein. The sac thus does not form the communication between the vessels, although the probe passes readily from either into it; nor are they directly united, but rather by way of a small space or vestibule which lies in front of the orifice of the sac. This sac is formed of dense fibrous tissue and is lined by a granular, deeply pigmented clot. The veins were enormously distended both below and above the level of the communication. The stagnation was such that the man suffered for many years from a persistent leg ulcer.

Operative interference is seldom advisable in such cases on account of the risk of gangrene.

Dr. Osler.—The question of operation is a very interesting one. You may remember that by a curious coincidence the other day upon which I showed this patient at the clinic I received a letter from an old friend, a patient of mine, who had had for many years an arteriovenous aneurism in the axilla. He was a man of 43, who when 15 years of age was running down a steep grade with a lead pencil in his pocket and it penetrated his axilla. He had a sudden redness and then blackness of the hand with the gradual growth of an aneurism, and he has had that aneurism ever since. He is a strong, vigorous man. He has had the day fixed for operation, but I think wisely, deferred it. The great danger of operating is in the gangrene which is apt to follow. A very interesting case was reported a short time ago by a Spanish surgeon, who in a case of this kind opened the artery, stitched the orifice and closed it up again and the man made a complete recovery.

Survey of Ovariotomy at Extremes of Life. Report of a Case in a Child aged Five. Mr. H. I. Wiel.

(See this Bulletin, page 102.)

NOTES ON NEW BOOKS.

A Text-book of Human Physiology. By ALBERT P. BRUBAKER, A. M., M. D., Professor of Physiology and Hygiene in the Jefferson Medical College; Professor of Physiology in the Pennsylvania College of Dental Surgery; Lecturer on Physiology and Hygiene in the Drexel Institute of Art, Science, and Industry. With colored plates and 354 illustrations. (*Philadelphia: P. Blakiston's Son & Co., 1012 Walnut St., 1904.*)

At a time when contributions to the subject of physiology are being made with unprecedented frequency, contributions containing facts not alone of a supplementary but often also of a revolutionary character, it becomes the duty of a writer of a text-book to select from the mass of conflicting data facts that are the most important and fundamental. These should be treated of fully but with the avoidance of unessential detail. At the same time every effort should be made to preserve the spirit of the subject, the spirit of a live science, and to instill it into the reader.

The following quotation taken from his preface bears witness to the fact that the author has borne in mind the necessity of sifting the essential from the unessential. "The object in view in the preparation of this volume was the selection and presentation of the more important facts of physiology, in a form which it is believed will be helpful to students and to practitioners of medicine." This we believe the author has in a large measure succeeded in accomplishing. It is of course manifestly impossible for different individuals to agree in all cases upon the phases of the subject that are to be considered the most important. In the opinion of the reviewer the author has in most instances used excellent judgment. Furthermore, it is particularly gratifying to find that the latest important work in all fields, but particularly in the fields of digestion and absorption, has been incorporated in the text.

But it is disappointing to find that the subject-matter has been handled just as it has in the past been handled by most English-speaking authors. No significant references to original articles are given and but very few names are mentioned. Those that do appear are almost exclusively names of Americans. The impression is therefore conveyed to the uninformed reader that almost the whole subject of physiology has been evolved from the brain of but a single individual. The objection might be raised by the writers of text-books that the introduction of names into the text and the historical development of our only too uncertain knowledge detract from what all must acknowledge to be the most important object of a text-book, namely a clear presentation of the facts. However, in the experience of the reviewer references to such points do not hamper the average student and under any circumstances they give the subject its true aspect, and increase the interest of the intelligent reader in it.

It is hardly necessary to dwell upon the general arrangement and scope of the book. The subject-matter is subdivided into chapters in the way that is usual in text-books of physiology intended for medical students. The "chemic" side of the subject is unusually brief. Perhaps the author intended this part of the book to be supplemented by a special course in "physiologic" chemistry. However, this cannot be said of the introductory "anatomic" descriptions. These are always full, particularly the one that has to do with the central "nerve" system. The "physical" aspect of the subject is likewise fully treated.

First Report of the Wellcome Research Laboratories at the Gordon Memorial College, Khartoum. By the Director, ANDREW BALFOUR. M. D., B. Sc. (*Department of Education, Sudan Government: Khartoum, 1904.*)

Readers who are familiar with Kipling's poems may remember that in one of them, called "Kitchener's School," the changes to be brought about in the Soudan after its occupation by Kitchener's army are foretold. One of the verses is as follows:

"He said 'Go safely, being abased. I have accomplished my vow.'
That was the mercy of Kitchener. Cometh his madness now!
He does not desire as you desire, nor devise as ye devise;
He is preparing a second host—an army to make you wise!"

The battle of Omdurman was fought in 1898, and now in 1904 we have the first report of the Wellcome Research Laboratories of the Gordon Memorial College at Khartoum. There could probably be no stronger example of the better influences of civilization.

Perhaps the most interesting articles are those in reference to mosquitoes. There is one dealing with the varieties of mosquitoes found in Egypt and the Soudan and the description of the work which is being done for their destruction. Insects and parasites injurious to crops are also considered and there is a section dealing with the general routine work of the Laboratory. The incidence of bilharzia is of special interest. Leprosy is noted as being comparatively common; they have also had an epidemic of cerebro-spinal fever. Tuberculosis is stated to be frequent and lues very prevalent, the more serious luetic lesions being apparently very common.

This first report is an excellent one considering the difficulties which had to be surmounted, and we shall look with interest for further work from this laboratory.

Records of the Egyptian Government School of Medicine. Volume II. Edited by the Director. (*Cairo: National Printing Department, 1904.*)

This volume contains a number of papers, some of which are of considerable interest. Dr. Phillips gives the record of one hundred consecutive cases of ascites in a Cairo hospital and discusses the causal factors, laying special stress on the rôle played by malaria. He notes the large number of cases of ascites in the hospital wards and this in a locality where but little alcohol is drunk. He is inclined to lay great stress on malaria as a causal factor, and out of his one hundred cases considers that in twenty-two this was definitely established. In twelve other cases the diagnosis is doubtful. If proved, these are exceedingly interesting findings and quite contrary to the experience of this country, where malaria is not regarded as an important causal factor of cirrhosis of the liver. On going through the details of these cases it does not seem that Dr. Phillips has sufficient evidence on which to base a diagnosis of malarial cirrhosis of the liver.

There is an interesting article on some of the unusual manifestations of bilharzia, especially with involvement of the abdominal viscera. Dr. Milton gives a more general description of bilharziosis.

An article of considerable interest is a description of the customs and superstitions of the modern Egyptians connected with pregnancy and childbirth. The volume concludes with a well-illustrated article on the morphology of the human brain, with special reference to that of the Egyptians.

Altogether the volume is a very creditable one. It would seem advisable, however, to have such reports in a volume of smaller size. A folio is not very convenient for ordinary reading.

A Text-Book of Human Histology. Including Microscopic Technic. By DRS. A. A. BÖHM, and M. VON DAVIDOFF, of Munich, and G. CARL HUBER, M. D., Professor of Histology and Embryology in the University of Michigan, Ann Arbor. Second Edition, Thoroughly Revised and Enlarged. Handsome octavo of 525 pages, with 376 original illustrations. (*Philadelphia, New York, London: W. B. Saunders & Co., 1904.*) Flexible Cloth $3.50 net.

The Böhm and von Davidoff text-book of histology has since its first appearance been a favorite with students who read German.

And the translation, edited and extended by Dr. Huber is even more deserving of a similar reception by English-reading students. The book though elementary is comprehensive—and the descriptions are accurate and clearly put, and do not bear the ear-marks of a translation. The work as a whole is well-balanced and no hobby is ridden to an extreme to the exclusion or curtailing of more important subjects. Nor do unsettled questions receive dogmatic answers. The illustrations are numerous and in the main of advantage to the reader. One regrets that in this second edition the list of references has been omitted—on account of lack of room. The few extra sheets necessary would by no means make an unwieldy volume, and if it did a little economy in descriptions of microscopes, microtomes, etc., would restore the equilibrium and give a more valuable book to the student.

A Manual of Personal Hygiene. Proper living upon a Physiologic Basis. By American Authors. Edited by WALTER L. PYLE, A. M., M. D., Assistant Surgeon to the Wills Eye Hospital, Philadelphia. Second Edition, Revised and Enlarged. (*Philadelphia, New York, London: W. B. Saunders & Co., 1904.*)

This is a useful and well-written book and we are gratified to know that it has attained a second edition. The need of such a manual is apparent to any one who examines the inquiry columns of any newspaper which replies to inquiries as to health and hygiene. The possession of the book would render most of these questions unnecessary. It is well printed and well illustrated. The language is simple and clear.

A Manual of Experimental Physiology for students of Medicine. By WINFIELD S. HALL, Ph. D., M. D. (Leipsic), Professor of Physiology, Northwestern University Medical School. With 89 illustrations and a colored plate. (*Philadelphia and New York: Lea Brothers & Company.*)

The appearance of a really good manual of experimental physiology is always greeted by the advocates of the experimental method with a feeling of satisfaction. The possession of a good laboratory guide by the student is of advantage not only to the student himself but also to the instructor who is thereby relieved from much of the tedium of repeating again and again the same directions and urging again and again the same warnings.

From the preface of Prof. Hall's new book, we learn that the author has, up to the present, furnished his class with typewritten syllabi of their laboratory exercises. These syllabi, having been revised almost annually, constitute the present volume, which, therefore, represents the accumulated experience of some ten years of teaching.

The point of view of an author is usually indicated by the space which he allots to the various subdivisions of the subject treated by him. Consequently the following data are not without significance:

	PAGES.		PAGES.
Muscle-nerve	35	Digestion, etc.	21
Circulation	27	Nervous system	15
Vision	27	Cytology	15
Hæmatology	27	Muscular system	5
Respiration	21		
		Total	240

Here one sees well exemplified the excellent and growing tendency to diminish the amount of "frog work" and to substitute for it experiments on man and the mammalia, for the part of this work devoted to the physiology of nerve and muscle is but one-eighth of the whole. Urine examination and Physiological Chemistry (with the exception of experiments in digestion) are not included in the volume but a number of experiments on the action of drugs are described. For the latter Prof. Hall expresses his indebtedness to Prof. C. H. Miller.

The nine chapters into which the book is divided may now be considered in turn:

I. *Cytology* comprises a brief study of the algæ and protozoa, also of the action of cilia both under normal conditions and under the influence of Co_2 and anæsthetics. Finally the method of estimating the amount of work done by cilia is described.

II. *Muscle and Nerve* includes a helpful explanation of the electrical apparatus usually employed accompanied by a number of simple schemata showing the arrangement of electrical connections.

III. *Circulation.* The insertion here by the author of a number of simple experiments in hydrodynamics, as an introduction to the study of the circulation, is to be commended. Considerable emphasis is laid on the mammalian vivisections; not only are the actions of the vagus and sensory nerves studied but also the effects of atropine, pilocarpine, digitalis and other drugs are observed. Some objections might be raised to the author's use of the term "pulse pressure," by which he designates the systolic pressure as determined by feeling the *pulse* at the wrist (Riva-Rocci method).

IV. *Respiration* describes some experiments on the effect of varying the composition of the inspired air. The respiratory quotient is also determined. One misses, however, an adequate consideration of the action of the afferent nerves (especially of the vagus) upon the respiratory center, although the function of the phrenic nerve is carefully studied.

V. *Normal Hæmatology* is the work of Dr. C. J. Kurtz. The usual methods of blood counting and hæmoglobin estimation are described. Among the latter one finds no mention of the most accurate of all, Miescher's modification of von Fleischl instrument. Differential counting is aided by a plate picturing the various forms of blood corpuscles.

VI. *Digestion and Absorption.* As a somewhat novel feature, one finds here a number of experiments such as those on the diffusibility of proteids illustrating the physical basis of absorption.

On VII, *Vision*, no comment need be made.

VIII. *Nervous System* treats of reflexes, skin sensibility, functions of the dorsal and ventral roots, effects of strychnia, curare, and veratria, etc.

IX. *Muscular System* deals with observations on the movements of man and with ergography. The value of the former may be questioned, while the ergographic experiments of students are usually regarded as unsatisfactory.

The *Appendix* contains practical hints regarding various supplies, appliances and methods.

"The proof of the pudding is in the eating," and it is not for one who has not employed Prof. Hall's book in his classes to speak authoritatively upon its value but careful perusal of the work will, it is thought, convince the reader that this manual possesses substantial merits.

Physician versus Bacteriologist. By PROF. DR. O. ROSENBACH of Berlin. Authorized Translation from the German by DR. ACHILLES ROSE. (*Funk & Wagnalls Company, New York and London, 1904.*)

Scientific papers usually consist of two parts; first, records of observations or statistics, and second, opinions or conclusions drawn by the writer from the given data. Consequently there are opportunities for error, both in observation and judgment. Many errors undoubtedly arise from deducing too extensive conclusions from insufficient observations. It is much easier to think than to see, and still easier to talk than to reason.

Since this is true, it would be very remarkable if, in the rapidity with which certain branches of medical knowledge have advanced, especially the science of bacteriology, errors should

not have arisen, which only further observations have corrected, or which are still generally regarded as truths.

To any one who wishes to set the scientific world right two methods are open, either the recognition of the generally accepted observations as correct and the demonstration of errors in reasoning by which conclusions have been deduced from them, or the presentation of new facts which in themselves are evidence of previous faulty observations or disprove the previous conclusions. And these new facts must consist of specific instances and not of broad generalizations based on the critic's impressions.

Attacks on conclusions with new conclusions by one who offers no new facts or only broad generalizations do not usually carry strong conviction. It is for this reason that the attack of Prof. Rosenbach on the bacteriologists will have little effect.

The chief thesis of the writer seems to be that bacteria are not the ultimate cause of most of the infectious diseases, but that predisposition is the important factor, bacteria playing entirely a secondary and unimportant rôle. But it is not the *physician* alone who lays stress on predisposition. In fact, pure bacteriologists have long recognized its importance and have adduced much experimental evidence in relation to it.

Many of the papers comprising the volume have appeared before, some of them at a period somewhat remote, so that at present they have lost much of their force. This is true of the paper attacking the therapeutic value of tuberculin, though we doubt very much whether this paper had much share in establishing the opinion at present generally held. On the other hand time has not shown the truth of the writer's opinion in regard to diphtheria antitoxin and no evidence or arguments are presented sufficient to change our opinions.

It is impossible here to enter into a discussion of all the views advanced by the writer. Suffice it to say that most of them are at variance with views currently accepted in regard to the relation of bacteria to disease. To those unfamiliar with the previous writings of this author it will be somewhat of a shock to find a German professor advancing such unusual opinions. But every man has a right to his opinion, and that of a man who has formerly done important work in pathology should receive a hearing. In a number of points discussed the last word has not yet been spoken and any new light should be gladly welcomed. We cannot see, however, that anything really new has been added to the subject by this book.

On almost every page are dogmatic statements entirely unsupported by evidence, while in places the most visionary theorizing is indulged in which might delude the undiscriminating reader. All this is concealed in a mass of words which rival the most obscure passages of Henry James; for example: Predisposition "depends upon the primary stimulability of the protoplasm, *i. e.*, upon the extent of innate faculty of causation which is identical with the primary (intra-molecular) combination of the atoms, and upon the extent of the at-all-possible transposition of energies, which is identical with the intermolecular power of combination, by which the molecules of different qualities are united into one aggregate of molecules!" (p. 84).

Just why there should be such a serious enmity between the physician and the bacteriologist is not made perfectly clear. The author writes, however, "And not only those (evidences) which the physician, endangered in his possessions, is justified in bringing forward to secure his rights, in opposition to the demands of the bacteriologists (who dare to direct the course of this world from their official table and to ignore well established facts), but also proofs of the social and ethical dangers which would arise from an absolute supremacy of bacteriology." No wonder that the physicians should challenge such bacteriological monsters!

The bacteriologists whom the author challenges apparently have no sense of modesty, for they "by means of fallacious conclusions, have established—in opposition to all common sense—the dogma that all infectious diseases are caused by bacteria." We should like to meet with some of these enthusiastic bacteriologists. We cannot see that any good can come from a book written in such an attitude of mind.

The translator has performed a service of doubtful utility fairly well. In our judgment he had better have left it undone. No good can come of it and harm may result, though it is doubtful if the book can have much influence.

International Clinics. A Quarterly of illustrated Clinical Lectures and especially prepared Original Articles on Treatment, Medicine, Surgery, Neurology, Pediatrics, Obstetrics, Gynecology, Orthopedics, Pathology, Dermatology, Ophthalmology, Otology, Rhinology, Laryngology and Hygiene. Edited by A. O. J. KELLY, M. D. Volume IV. Thirteenth Series, 1904. (*Philadelphia: J. B. Lippincott Company, 1904.*)

This volume, as did the preceding ones of the series, contains articles by well-known medical writers in all parts of the world. Their chief value seems to the reviewer to lie in the fact that they present the personal views and experiences of the writers. It is not claimed that they are exhaustive treatises on the subjects considered, but are short papers, usually written in an informal, almost conversational style. Most of them, as is intended, leave the same impression on the reader as though he had attended the author's clinic. Considered in this way, they furnish most attractive reading.

In the present volume appear short papers by Sir Dyce Duckworth, J. Chalmers Da Costa, W. W. Keen, Nicholas Senn, J. N. Musser, James Tyson and many others.

The clinical features and treatment of ulcer of the stomach are considered by Prof. Tyson. It is interesting to read this author's views in regard to the question much discussed at present concerning operative procedures in unperforated gastric ulcer. The writer's one experience with operation, of which he says "the result could not have been worse if the operation had been left undone," makes him hesitate to advise operation. "The offsets to the operation," he says, "are, first, the very slight mortality from ulcer, even when there have been many hæmorrhages, and second, the seriousness of the operation." Certainly the opinion of one who has had such a large medical experience should have weight with some who advise exploration of the stomach on almost any pretext.

Prof. Musser discusses "The treatment of pneumococcus infection of the lung, or croupous pneumonia." Nothing very strikingly new appears here though it is of very great interest to learn this clinician's exact method of handling this serious disease. Of importance is the slight use of alcohol in this disease by Prof. Musser, and also the stress he lays upon the value of venesection in certain cases, though he does not urge this so strongly as do some German teachers.

Prof. Julien, of the University of Paris, writes regarding the "Subcutaneous injections of mercury for syphilis," of which method of administration he has long been an advocate, but which has not been largely employed in this country. He discusses quite fully the relative values of the different preparations of mercury for this purpose and the exact methods for their administration.

A very interesting little paper, of only five pages, by Sir Dyce Duckworth on "The importance for students of physiognomical diagnosis in disease" should be taken to heart, not only by students, but also by teachers of medicine. He begins by quoting a favorite maxim of the late Professor Humphry of Cambridge, "Eyes first, eyes second, and hands third."

Probably the most interesting surgical paper is one by Professors Keen and Da Costa on "A case of inter-ilio-abdominal amputation for sarcoma of the ilium, and a synopsis of previously reported cases." The writer's case is most carefully described

and a full account of the operation as performed, showing the important modifications from the previous operations, is given. The fact that the result in this case was unsatisfactory, death occurring in 33 hours, does not detract from the value of this report to all who may be interested in these extensive operations.

Dr. McFarland discusses the present state of our knowledge of immunity and, while he has given a very interesting résumé, its brevity and conciseness prevent its being of much value except to those who are already conversant with the subject.

We are not able to mention even all the excellent papers which this volume contains. It is not to be expected, however, in a book of this kind that all of the articles should be of equal merit. One must confess that some of them read suspiciously like "space-fillers." The many good papers, however, more than compensate for hastily written and somewhat stereotyped productions.

The Infectivity of Enteric Fever. With observations on its origin and incidence at Caius College, Cambridge, Festiniog and Wicken-Bonaut. By ALEXANDER COLLIE, M. D. (Aberd.). (*Bristol: John Wright & Co. London: Simpkin, Marshall, Hamilton, Kent & Co., Lt'd., 1904.*)

This is a small pamphlet of forty-seven pages, in the preface of which it is stated that, "The writer's aim is to demonstrate that enteric fever is an infectious disease, communicable by direct personal intercourse, just as typhus fever is, and that explanations of its origin from drinking water have in several instances, failed in the ablest hands."

It is evident that the writer uses the term infectious much in the sense that contagious is generally understood. Certainly he would now need to search far to find one who does not already believe that enteric fever is *infectious*.

In evidence of its direct communicability the writer reviews the course of three epidemics occurring at Festiniog, Wicken-Bonaut, and Caius College, Cambridge. These epidemics occurred in 1863, 1869 and 1873 respectively. Certainly this epidemic based on epidemics occurring over thirty years ago, which apparently were not very thoroughly studied at the time, and the opinion concerning which now given by the writer being in direct variance with that given by the medical officer commissioned to examine it at the time, cannot be considered a strong support to the view that typhoid fever is frequently transmitted directly from patient to patient.

The book is chiefly interesting as one concerning typhoid fever, published in 1904, in which the typhoid bacillus is not mentioned and in which the first argument is that sewer-gas plays no rôle in the etiology of this disease! The pamphlet would have been obsolete twenty years ago.

To those, however, who feel that this direct mode of transmission of typhoid fever is of more importance than is usually ascribed to it, that "food, fingers and flies" play a considerable share in its spread, one or two statements of the writer are interesting. The Homerton Fever Hospital was opened for small-pox on the 15th of February, 1871, and closed for that disease on the 15th of the following June. During that time 1194 cases of small-pox were admitted. The staff consisted of about 100 persons. Among all these persons not a single case of enteric fever occurred. In October, 1871, the hospital was opened for fever cases and from that time up to the year 1878, 21 cases of enteric fever occurred amongst the staff.

Also from February 1, 1871, to September 19, 1879, 6771 cases of small-pox and 171 of scarlet fever had been treated in the Homerton Small-pox Hospital; and during this time 487 persons had been employed in attendance upon the sick and otherwise; but during all that time no case of enteric fever had occurred among these 7000 persons. On September 29, 1879, that hospital was opened for enteric fever, and within six weeks there were two cases among the nurses who nursed it, followed by a third a little later and by a fourth at the end of three months.

The Surgical Treatment of Bright's Disease. By GEORGE M. EDEBOHLS, A. M., M. D., LL. D. (*New York: Frank F. Lisiecki, 1904.*)

This book consists of the various papers on this subject published by Dr. Edebohls, followed by the histories of the patients operated on up to the end of the year 1903. There is also an analysis of all his cases and the results.

The value of the surgical treatment of chronic nephritis is of great interest to the profession; regarding it we would all wish to come to a definite opinion. For this, it is important to have as large a series of cases reported as possible, but if these reports are to be of value it is necessary that they be thorough and accurate. In connection with this it is a matter for regret that Dr. Edebohls' records are not more complete. This is especially the case in regard to the vascular conditions. Thus for example in Case 22 it is stated that the patient had enormous hypertrophy of the heart and general arterio-sclerosis. Fourteen months afterwards it is stated that his heart was found normal. This change may have occurred but it seems very unlikely, and it is a great pity that exact measurements are not given. If enormous hypertrophy can disappear in this way it is an exceedingly interesting clinical fact. Another curious clinical observation is a statement of the observation of an intermittent aortic regurgitant murmur occurring every third, fourth or fifth beat or even less frequently. Dr. Edebohls would be doing a great service to clinical medicine if he would report a series of these cases, as the majority of clinicians are quite in ignorance of any such condition.

Dr. Edebohls reports seventy-two cases, of which seven died within two years after the operation, and twenty-two died some time later. Of the forty-three survivors the result was unknown in three, unimproved in twenty, and cured in seventeen. In dealing with the results of any procedure in the treatment of chronic nephritis one has always to keep in mind that under ordinary medical treatment patients who are apparently at the point of death may recover and enjoy good health perhaps for many years. Such cases are by no means rare and one has to bear this in mind in discussing the results of any form of special treatment. In discussing both the group of improved and cured cases it seems that Dr. Edebohls rather loses sight of this point. Thus many of the cured cases occurred in very anæmic women, and one cannot but feel that in many of these under other treatment the results might have been equally good. The same criticism applies to cases occurring after pregnancy. It is curious to notice that in his report of cases *after* operation Dr. Edebohls is inclined to minimise the importance of a trace of albumen. Would he do so *before* operation? There is one group of cases regarding which further study will be needed, those characterized by the arterio-sclerotic kidney. It is difficult to recognise this group in Dr. Edebohls' cases. It is to be hoped that in future work special attention will be directed towards them. It is interesting to see Dr. Edebohls' experience of the operation on patients with albuminuric retinitis. They all died within a year after operation. Only two experienced decided benefit. Among the cases reported as cured many are noted as having very movable kidneys. This may give conditions suggestive of nephritis but it is doubtful if the diagnosis is justified in all cases.

The impression gotten from this book is that undoubtedly there seems to have been improvement in certain cases following operation. That such is the case there is little question. As to the possibilities of permanent cure we do not feel convinced by Dr. Edebohls' cases. There is one important point which he has brought out, that one kidney only may be diseased and the other apparently normal. It may be that many of the cases of albuminuria, especially in young subjects, are due to this latter con-

dition. The after-history of such cases will be especially important. In the examination of portions of kidney tissue removed with the capsule too much importance should not be given to slight degenerative changes. In the majority of persons over thirty an occasional sclerotic tuft and some increase in the fibrous tissue can be found.

If Dr. Edebohls wishes to convince the profession of the curability of chronic nephritis by operation (and we would only too willingly be convinced), he must try to present his evidence in more convincing form. Where one finds careless clinical observation in regard to one set of organs one can but hesitate as to the interpretation of the conditions in another system.

Saunder's Question Compends. Essentials of Materia Medica and Prescription Writing. By HENRY MORRIS, M. D., College of Physicians, Philadelphia. Sixth Edition. Thoroughly revised. By W. A. BASTEDO, Ph. G., M. D., Tutor of Materia Medica and Pharmacology at the Columbia University (College of Physicians and Surgeons), New York City. (*Philadelphia, New York, London: W. B. Saunders & Company, 1904.*)

If a book derives its value from the title, then this one should have it increased three-fold, for it is called:—"Essentials of Materia Medica and Therapeutics," "Essentials of Materia Medica and Prescription Writing," and "Essentials of Materia Medica, Therapeutics and Prescription Writing." All these titles combined go to make up a compact volume that has for many years been of good service to the student. The great improvement in the present edition should be welcomed with delight.

It is very difficult to carry compression of Materia Medica and Therapeutics to any great extent without sacrificing completeness of subject and clearness of definition. Yet the revisor has accomplished this in admirable style as the answers to the questions, of which the book consists, are clearly and tersely expressed.

Under the subject of Weights and Measures, the Metric system is not treated as practically as it should be. The information given would hardly induce a physician to adopt the system for prescription writing. Prescription writing occupying such a conspicuous place, as a part of the title of the book, more space should have been devoted to the subject. Generally speaking, I am sorry to say proper prescription writing seems to be losing its importance.

The definitions, arrangement and classification of the book could not be better. The classification is such that referring to the contents, one can at a glance see all the drugs under the proper headings. For instance, under the heading "Medicine acting on the Alimentary Canal" will be "Emetics, Gastric Sedatives, Carminatives and Cathartics," the various drugs following each subject. This arrangement being carried out throughout the book makes it of great value to the student for review work.

Mental Defectives, their History, Treatment and Training. By MARTIN W. BARR, M. D., Chief Physician Pennsylvania Training School for Feeble-Minded Children, Elwyn. Illustrated by 53 full page plates. (*Philadelphia: P. Blakiston's Son & Co., 1904.*)

This is a useful book and contains much that every physician should know about idiocy. The history of the philanthropic movement which in every land fostered, during the past century, the establishment and growth of institutions for the education of the feeble-minded is entertainingly told in a chapter of somewhat more than fifty pages. The author's attempt at classification is from an educational stand-point and strangely enough fails to distinguish physical states. He also employs the term moral imbecile—as if there could be a moral deficiency over-shadowing the mental defect. In all so-called moral imbeciles the arrest of mental development must be the primary condition, and the defect of the moral sense cannot be considered a condition by itself. Moral imbecility so-called is simply one of the symptoms of a fundamental mental deficiency.

The chapter on etiology is full and comprehensive. The influence of heredity is also given due weight in a discussion of this important factor in arrested mental development.

The chapter entitled "Training and Treatment" is the most valuable in the book and should be carefully read by all who have to do with defective children. In fact every teacher of children would profit by a study of the methods employed to secure the mental development and training of backward or slow children.

Idiot savants also receive a due share of attention and many striking instances of one-sided mental development with remarkable special powers are mentioned.

The book is undoubtedly the best which has been published in America. There are certain faults of arrangement which mar its unity and give one the impression that it is a collection of monographs on special topics, rather than a systematic treatise.

The concluding sentence of the Foreword (Preface?) deserves to be reproduced in this connection. "In this last (the preparation of the book) my three boys have materially contributed in addition to the aid gladly and efficiently rendered in the preparation of the book; many of the photographs by Jake, the translations by Arthur and the entire typewriting of the manuscript by Judson, all being an exposition of the main argument—the possibilities to be attained through training."

Diseases of the Nose, Throat and Ear. By SETH SCOTT BISHOP, M. D., D. C. L., LL. D. Third edition, thoroughly revised and enlarged. Illustrated with ninety-four colored lithographs and two hundred and thirty-two additional illustrations. 564 pages. (*Philadelphia: F. A. Davis Co., 1904.*)

This book is a fairly acceptable text-book for students who have but little time to devote to these specialties. The parts devoted to therapeutics are especially complete. It is to be regretted that the author has so incompletely described the diseases of the accessory sinuses and their treatment. The recent typical rhinological operations for correction of deviations of the septum, devised by Krieg and Freer are not mentioned. The book is attractively bound and printed. It contains numerous illustrations of specimens, instruments and apparatus.

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CONTENTS.

PAGE

The Surgery of the Posterior Mediastinum; its Past and its Future. By J. D. Faure, M. D., ... 125

Aplastic Anæmia Associated with Lymphoid Hyperplasia of the Bone-Marrow. By George Blumer, M. D., ... 127

Preliminary Communication Regarding an Immune Body Capable of Inhibiting the Development of Cancer in Mice (Adeno-Carcinoma, Jensen). By G. H. A. Clowes, Ph. D., ... 130

A Multiplex Slide-Holding Device. By Edward F. Miller, . . 132

Dr. Heinrich or Henry Keerl, of Baltimore, the "Hessian Surgeon." By Eugene F. Cordell, M. D., ... 133

The Bacillus Aerogenes Capsulatus in Puerperal Infection. By Herbert M. Little, M. D. 136

PAGE

Proceedings of Societies:

The Johns Hopkins Hospital Medical Society, ... 146

A Case of Arterio Venous Aneurism [Dr. Osler];—The Immunization of Mice to Cancer [Dr. G. H. A. Clowes];—Pathological Changes [Dr. Welch];—Apparatus for the Treatment of Fracture of the Femur; Treatment of Esophageal Stricture [Dr. Theodore Dunham];—Peri Pancreatic Abscess [Dr. Thayer; Surgical Treatment, Dr. Finney];—Gastric Tetany [Dr. Howard];—The Pathology of Tetany [Dr. MacCallum;—Synæsthesia [Dr. H. L. Smith];—Hanging Block Cultivation of Bacteria; The Ultraviolet Rays; Thermophilic Bacteria [Dr. Ford];—The Cure of Uterine Cancer [Dr. John G. Clark];—Pathology of Cervical Cancer [Dr. Sampson].

Notes on New Books, ... 150

THE SURGERY OF THE POSTERIOR MEDIASTINUM; ITS PAST AND ITS FUTURE.[1]

By J. D. Faure, M. D., *of Paris, France.*

The revolution which gave to surgery a scope previously unknown and far beyond the dreams of our predecessors, has as yet failed to supply efficient means for the treatment of affections of the posterior mediastinum.

The fact that this region is situated in the depth of the chest between the lungs, before the vertebral column, and behind the bronchia and the superior part of the heart, has, until very recently made it unattainable, and protected it from invasion on the part of even the most daring surgeons.

When abdominal surgery was achieving all conceivable operations upon the uterus and its adnexa, the liver and the bile ducts, the spleen, the stomach, and the intestine; when the surgery of the chest ventured to incise the lungs in order to reach abcesses, or even to extirpate fragments of lung tissue; when the cranium and the vertebral column were opened in order to explore the nerve centers, and evacuate cerebral abscesses, or to extirpate tumors of the spinal cord or of the encephalon; when the anterior mediastinum was entered for the purpose of suturing wounds of the heart, the posterior mediastinum alone still remained inaccessible.

[1] Address delivered at the Johns Hopkins Hospital, April, 1904.

There were, it is true, many bold attempts at its surgery, all or nearly all of which attacked the esophagus either for cancer or for occlusion occasioned by a foreign body. I do not here take into account the few operations performed upon scrofulous abscess, which led surgeons as far as the anterior part of the vertebral column, because although they were actually operations on the posterior mediastinum, they achieved nothing more than the cleansing of a tuberculous abscess, and cannot be considered in the same light as the deliberate opening of that region for the purpose of operating upon the organs which it contains.

Operations of the latter kind have been very rare, and although, in 1888, Wassalow showed for the first time that it was possible to reach the esophagus by resecting a few ribs and separating the pleura from the costo-vertebral groove, the most important publications made since that date have been entirely anatomical. Quénu and Hartmann, and Potarea have investigated the connections between the esophagus and the thorax and demonstrated that in order to reach the former it is necessary to pass either by the left of the vertebral column (Quénu and Hartmann) or by the right (Potarea).

Schwartz has made some interesting researches on the means of reaching the bronchia in order to extract foreign bodies. Lery experimented in resections of the esophagus upon dogs, and Jowet utilizing the same animal, succeeded in affecting the trans-diaphragmatic anastomosis of the esophagus with the cardiac end of the stomach.

Operations upon the posterior mediastinum in human beings, undertaken with a therapeutic purpose, have been very rare. Relm attempted to extirpate cancer, but only succeeded in incising the esophagus. Slobet and Tuffier, the latter operating through the pleura, have also incised this organ, to relieve cicratricial stricture, and Forgue made an effort to extract a foreign body from it, but was obliged to abandon his attempt without opening the esophagus, succeeding only in exploring it with the finger tip. Curtis, in 1886, opened the right bronchus through the posterior wall in order to extract a foreign body, which, after all, he could not reach. Such, unless I am mistaken, are all the operations hitherto performed on the posterior mediastinum. They have all, as you see, been tentative and have ended in failure, or at least terminated in simple incision of the esophagus or the bronchi. However bold and skilful the surgeons who made these attempts may have been no other result was possible, at least in the case of operations upon the esophagus; bronchotomy, performed for the extraction of a foreign body might be successful, but operations upon the esophagus such as those just cited, were foredoomed to failure.

According to Wassalow's method, which all operators are now bent upon following, any extensive operations upon the esophagus are utterly impracticable. It is true that it is possible to reach it after the third, fourth, fifth, and sixth ribs have been resected and the pleura pushed aside, and after it is recognized and grasped with a pair of forceps, a foreign body, impacted at this level, can be extracted. It may also be possible to incise a stricture, but there is not sufficient space for extirpation of the esophagus. In fact, if extirpation is to be attempted, it is best to adopt the transpleural route with liberal opening of the chest, as indicated by Tuffier, though it is a great inconvenience to operate through the pleura and the risks of accident are multiplied by doing so. This method supplies more room, however, and although like those of Wassalow, Potarea, Quénu, and Hartmann it is perilous and difficult, it does not, at any rate, present impossibilities. It is insufficient, it is dangerous, and it is bad, but it is practicable.

For some time I have been strongly convinced that some better method might be devised, for I believed that it was not only possible but easy to open a clear wide pathway to the posterior mediastinum, affording sufficient space to permit the execution of any operation.

It seemed to me that I could best demonstrate this fact by performing the most difficult operation possible, and therefore I undertook the extirpation of a cancerous esophagus situated in what is held to be the most inaccessible region, that is the center of the posterior mediastinum, behind the bifurcation of the bronchia and the pedicle of the lung.

I succeeded in performing this operation without accident, and even without difficulty, and although both my patients died in consequence of unforeseen accidents I believe that I have, nevertheless, demonstrated the possibility of operating successfully on the only part of the human body from which surgeons have heretofore been withheld by a consciousness of impotency.

I do not insist that such operations must be performed exactly as they are described in the *Bulletin de la Société de chirurgie de Paris* for January 25, 1903, I only wish to insist upon the conditions which are essential to success. One of these is a means of access to the posterior mediastinum sufficiently wide to permit ease of movement and enable the operator to execute all the numerous delicate manipulations and explorations demanded in such an important operation. All surgeons have hitherto obstinately limited the extent of their original opening to the resection of three or four middle ribs, but this is too narrow a means of access and fails to give sufficient space and light. To enable the surgeon to see clearly and fully it is necessary to include the first rib in the costal resection, although this, for some inexplicable reason has heretofore been respected. It is the section of these ribs and particularly of the first one, however, that governs the conditions of the operation. So long as the first rib is intact it is impossible to make any extensive manipulation in the posterior mediastinum, and even if all the other ribs from the second to the eighth, or even the ninth be removed, the first rib still fixes the shoulder and all the adjacent parts of the chest immovably to the vertebral column; if, on the contrary, the first rib is resected or even simply divided, the corresponding half of the chest is immediately loosened from the backbone, while the shoulder is pushed aside to such an extent that it becomes necessary to hold it to avoid wrenching the roots of the brachial plexus. The posterior mediastinum then opens like a book, and nothing is easier, after detaching the pleura and the apex of the lung, than to reach its depths and execute all possible manœuvres. In my operations, conducted after this method, I have been able to explore the posterior part of the trachea and bronchia, to dissect the pneumogastric nerve behind the pedicle of the lung, and to make, in short, all the manipulations necessary to success in a complicated operation such as the extirpation of a part of the thoracic esophagus.

This new technic has brought the most difficult operations on the posterior mediastinum within the range of possibility. Only experience can show what a future is in store for them, but we are at liberty to speculate in regard to it.

It is, of course, evident that this class of operations must always be of a serious character, since the life of the patient is at stake, and they are indicated only in cases where all other means of treatment have been tried in vain and where life is in immediate danger, such as cancer, foreign bodies in the esophagus, or suppurative mediastinitis. In extracting foreign bodies retained in the bronchia, it seems to me that the

usual methods are best, using the Williams bronchoscope for the purpose, or if such means absolutely fail, a simple bronchotomy may suffice. But should the latter operation, which is somewhat obscure, prove unsuccessful, it is obvious that the enlargement of the restricted path afforded by resection of three or four ribs into a wide exploration by section of five or six ribs such as I practice and advise would be indicated as a last resource.

Suppurative mediastinitis, does not often, in my opinion, afford a suitable opportunity to try this final expedient. The signs of the condition are generally too obscure and its evolution too rapid, to render such intervention possible. Under certain conditions, however, it may be necessary to employ it.

The results obtainable in cancer of the esophagus is a question of importance. I do not entertain, with certainty, any hope that cancerous patients can often survive the extirpation of the esophagus many years. But I do not see why the operation should not sometimes be followed by a lasting success.

It is true that my two patients died, both succumbing in the same way after twenty-four hours, without hemorrhage and without fever, but with symptoms which may, I think, be ascribed to slow suffocation. I had thought it necessary to leave a large drain in the posterior mediastinum, and through this, as I could plainly see, a large quantity of air penetrated the mediastinum at each inspiration, producing a genuine extra-pleural pneumothorax, and so lessening, by just so much, the quantity of air entering the lungs. I have had no further opportunity to perform the operation, and to ascertain, as I intend to do, if the suppression of the drain will obviate the symptoms just described. If, as I think possible, this cause of death can be removed, I see no reason why the operation, although undoubtedly a serious one, should not yield results more successful than these to which I have as yet attained, thanks to the technical improvements which new operations always introduce.

Sauerbach (Mickulicz' assistant) has just developed upon animals a method which may, to a certain degree, avoid the accidents I have described as well as those which may result from pneumothorax. He operates in a hermetically sealed box, where a certain amount of vacuum is created. The head of the animal is kept outside. The surgeon and his assistants are inside the box, operating upon the body of the animal, the neck of which is set in a hermetically sealed rubber collar, which prevents communication with the outside air. The excess of pressure inside the lungs communicating with the outer air, on the pressure outside the lungs exercised by the rarified air of the box prevents accidental pneumothorax and allows, so its author claims, the execution of the most complicated operations within the thorax without any danger of opening the pleura. I earnestly wish this method may be successful, but I fear it is very difficult of application to man and I hardly expect to see it in use among surgeons. The point of present importance, in my opinion, is to guard against the danger of extra-pleural pneumothorax, occurring, as I have just described, and to prevent it by suppressing the use of drains.

It is, however, in the extraction of foreign bodies impacted in the thoracic part of the esophagus that posterior thoracotomy will, I hope, give its best results. Under these circumstances, when attempts to extract foreign bodies by the natural channels have failed, this form of thoracotomy should be the operation of choice. In spite of the best guiding marks, the simple resection of the middle ribs may not suffice for the discovery of a foreign body in the thoracic esophagus, and still more is it likely to fail in its extraction. This new technic will permit extraction without difficulty and with every prospect of success.

I should never advise this operation in the case of strictures of the esophagus due to cicatricial tissue. This condition can be relieved by means which are fully as efficacious and less dangerous. A patient whose esophagus has been removed can be perfectly well fed by the more harmless and perfectly sufficient gastrotomy.

The gravity and difficulty of the operation just described are such that it must be reserved, as I have said, for patients whose lives are in immediate danger from cancer or from the presence of a foreign body in the esophagus. I shall consider myself well repaid for my trouble if only one life is saved by means of it. Allow me to add that nothing could please me more than to see one of you perform the first successful operation of this kind.

APLASTIC ANÆMIA ASSOCIATED WITH LYMPHOID HYPERPLASIA OF THE BONE-MARROW.

By George Blumer, M. D.,

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[From the Pathological Laboratory of Cooper Medical College, San Francisco, Cal.]

Since Ehrlich[1] described the first case of so-called "aplastic" anæmia in 1888, a number of cases have been placed on record. Up to the time that Senator[2] reported his recent case many writers seem to have regarded the lesions underlying this condition as essentially uniform, though there has been a good deal of discussion as to whether these lesions were to be regarded as a specific pathological entity or merely as a subform of ordinary pernicious anæmia. There is certainly a striking difference between the narrow lesions in

[1] Charite-Annalen, 1888.

[2] Zeitschrift für klinische Medicin. Bd. LIV. Hft. 1 and 2.

Muir's case,[3] in which the marrow was aplastic and fatty throughout, and those in Senator's case, in which it was hyperplastic and lymphadenoid throughout. These cases again differ from those with the ordinary lesions of pernicious anæmia plus aplasia of the bone-marrow. The examination of the bone-marrow in many of the reported cases is comparatively imperfect, and it is therefore difficult to say, positively, under which type many of them are to be placed. As atypical cases are often of value in clearing up doubtful points, we venture to record a case which was observed in the service of Dr. J. O. Hirschfelder in the City and County Hospital. We are indebted to Dr. Hirschfelder for the opportunity to study the case. The following is a summary of the important points in the clinical and pathological history of the case:

P. D., male, a laborer by occupation, was admitted to the Hospital November 4, 1904, complaining of general weakness and shortness of breath.

His family history was negative. Aside from a definite history of an attack of lues thirty years ago his past history was unimportant. His present illness began one year and ten months prior to admission. He dated it from the passage of a considerable quantity of blood from the bowel as a result of hemorrhoids. Since then he has had occasional passages of blood, but only when constipated. As far as can be judged the quantity of blood lost in this way has not been great. Aside from his rectal trouble he has had no symptoms of note until eight months ago when he began to have gastric disturbances. Since that time he has vomited a good deal, at times as often as thrice daily. At no time has he vomited blood. At the same time he has suffered from a progressively increasing weakness and shortness of breath. He has lost ten or twelve pounds in weight since the beginning of the illness.

Examination shows a well developed and moderately well nourished individual with a distinctly yellowish pallor. The chest is fairy well formed. Aside from the usual physical signs of emphysema the lungs are negative. The area of cardiac dullness is not enlarged, and the heart sounds are clear. The second pulmonic sound is accentuated. The liver dullness measures 12 cm. in the mammillary line, the edge of the organ is palpable. The spleen is not palpable. The lymph nodes throughout the body are slightly enlarged. There is a projecting external hemorrhoid, and rectal examination shows a number of internal hemorrhoids and a sloughing ulcer on the right wall of the rectum.

Smears from the blood show slight variations from normal in the size of the red corpuscles. There are a very few macrocytes most of which show polychromasia. A moderate number of microcytes are seen. Poikilocytosis is present but not marked. An occasional red corpuscle shows granular degeneration. There is very evident leucopenia. The predominating type of leucocyte is the small mononuclear form, and 80% of these are typical small lymphocytes. The remainder differ from them only in slight irregularities of the nucleus, and in the possession of a greater amount of protoplasm containing an occasional basophile granule. Hardly any blood plates are to be made out. The following table shows the result of the blood counts:

	Reds.	Leuc.	Hb.	Poly.	L. Mono.	S. Mono.	Eos.	Bas.
5th			..	6.0%	4.5%	89.5%	0	0
7th	1,516,000	4,600	20%	10.3%	1.3%	88.3%	0	0
8th	1,304,000		20%	8.0%	1.5%	90.0%	0	0.5%
9th			..	7.5%	2.0%	90.5%	0	0
10th	1,100,000	2,450	..	7.5%	2.0%	90.5%	0	0
14th	1,204,000	4,200	22%	7.5%	2.25%	90.25%	0	0

[3] British Medical Journal, 1900, Vol. II, page 909.

An average of one nucleated red to each differential count was observed. The cells were all of the normoblast type, or but slightly aberrant. No definite megaloblasts were seen.

The stomach analysis shows an absence of free hydrochloric acid, a trace of lactic acid, and microscopically a few large bacilli.

The urine contains no albumen or sugar, microscopically a few leucocytes and a few granular casts are present.

The feces contain no parasites or ova.

During the time the patient was under observation there was an irregular temperature ranging between F. 100 and F. 103.5. The patient died thirteen days after admission with signs of bronchopneumonia.

The autopsy was made by Dr. Wm. Ophüls, three hours after death. The following notes are abstracted from the protocol:

Heart.—The pericardium contains 70 cc. of clear fluid. The heart muscle is dark brown and firm. The valves are normal.

Lungs.—There is marked diffuse emphysema. There are easily torn adhesions at the apex of the left lung, and a small scar in the lung beneath them. The upper part of the left lung shows localized œdema and hyperæmia. There is a small scar at the right apex. On the right side there are larger areas of œdema and hyperæmia, and some consolidated spots. There is an encapsulated caseous area a little below the right apex.

Liver.—The organ measures 16 x 27 x 6 cm. It is dark brown in color. Over the anterior part of the right lobe there is a circumscribed thickening of the capsule with a small scar in the liver tissue beneath. The gall-bladder is large, and filled with clear, light yellow bile containing a few dark flakes.

Spleen.—The organ measures 10.5 x 2.5 x 2.5 cm. The markings are very definite. There are some barely visible brown spots in the pulp.

Kidneys.—The left measures 11 x 5.5 x 3 cm. The capsule is firmly attached. The tissue is pale and slightly brown. Right kidney same as left.

Adrenals.—Both are small and dark brown in color.

Genitalia.—Marked atrophy is present in the external genitals. There are large white scars in both testes.

Stomach.—The organ contains thin yellow fluid. The mucous membrane shows slight atrophy.

Intestines.—The duodenum contains bright yellow contents. The jejunum is normal. There is marked atrophy of the ileum and colon. The upper end of the rectum is contracted. At the anus there are several external hemorrhoids, the largest 2.5 x 1.5 cm. Extending 5 cm. up the rectum is a large irregular ulcer with partly brown, partly yellow necrotic masses at the bottom. At one place the ulcer has perforated into the peri-rectal fat.

Aorta.—There are a few yellow spots in the intima.

Lymph Nodes.—There are some moderately enlarged, reddish-gray lymph nodes in the supra-clavicular space. The peribronchial lymph nodes contain calcified areas. The retroperitoneal hæmolymph glands are slightly enlarged, and dark red in color.

Bone-marrow.—The bone-marrow in the upper part of the right tibia is yellow and fatty. There is partly red and partly yellow marrow in the upper end of the left humerus and the lower end of the left femur. The vertebral marrow shows no marked change to the naked eye.

Bacteriologic.—The cultures from the lung show the diplococcus lanceolatus associated with the bacillus of Friedländer and the bacillus pyocyaneus. The cultures from the liver, spleen, and kidney show the bacillus pyocyaneus with the colon bacillus.

The following were the important points brought out by the histologic examination:

Heart.—The right ventricle shows a moderate degree of fatty infiltration. The left ventricle shows well-marked brown atrophy.

Lungs.—The usual appearances of emphysema, œdema, and hyperæmia are present. In the consolidated areas the lesions of broncho-pneumonia are found, the predominating cells in the exudate being polynuclear leucocytes.

Liver.—Marked brown atrophy is present. The pigment, which is present in considerable amount, follows the course of the bile capillaries. It does not give the iron reaction.

Spleen.—There is periarteritis of most of the splenic vessels. The lesions of chronic passive congestion associated with an early chronic interstitial splenitis are present. There is a little brown pigment in the pulp which does not give the iron reaction.

Kidneys.—Both kidneys show a few patches of atrophy in the cortex. There is a moderate degree of cloudy swelling.

Testicles.—There is atrophy of the glandular tissue associated with patches of dense scar tissue.

Stomach.—There is a moderate degree of atrophy of the mucosa.

Intestines.—The mucous membrane of the ileum shows a moderate degree of atrophy. The ulcer of the rectum shows a base made up of granulation tissue; this is capped by a necrotic layer in which a few polynuclear leucocytes are present.

Lymph Nodes.—There is slight hyperplasia. The hæmolymph glands do not show any evidence of increased blood destruction.

Bone-marrow.—Smears from the tibia showed only blood having the same characteristics as that from the peripheral circulation. Smears from the vertebral marrow show a marked hyperplasia of the lymphoid elements, and almost complete absence of nucleated reds. The predominating cell is a mononuclear element about the size of the small mononuclear cell of the circulating blood. This cell has a large, pale-staining, centrally-situated nucleus, with a narrow rim of protoplasm which stains but little darker than the nucleus, and is at times scarcely distinguishable from it. Granular cells are almost absent, those most numerous being mononuclear cells with small, thickly-clustered, basophilic granules. Nucleated reds are very scarce, only 15 being seen in a count of 3200 cells. These were all of the normoblastic type. A count of 3200 cells gives the following:

Small Mononuclear cells	98.52%
Large Mononuclear cells	.28%
Polynuclear leucocytes	.03%
Polynuclear eosinophiles	.03%
Neutrophile myelocytes	.18%
Basophile myelocytes	.21%
Atypical forms	.75%

The sections of the bone-marrow confirm these findings. The marrow from the tibia consists entirely of fat; that from the lower end of the femur, and from the vertebra shows marked lymphoid hyperplasia, most marked in the vertebral marrow. In both of the last named sections the almost complete absence of nucleated reds and granular leucocytes is apparent.

From a clinical standpoint this case presents all of the leading characteristics of progressive pernicious anæmia: the yellow anæmia without much emaciation, the gastro-intestinal symptoms, the progressive weakness and dyspnœa, and the lack of physical findings. Yet neither the blood picture nor the pathological findings correspond to those of ordinary pernicious anæmia. The blood, in fact, shows none of the changes which are ordinarily found in pernicious anæmia except the progressive character of this anæmia, and the leucopenia with the relative increase in the mononuclear leucocytes. The great variation in the size of the red cells, the presence of megalocytes and megaloblasts, and the high color-index are lacking. The picture presented corresponds to that originally described by Ehrlich in 1888 as "aplastic" anæmia. As the name indicates there is, in such cases, a lack of evidence in the blood of any attempt on the part of the bone-marrow to compensate for the loss of blood corpuscles. The picture presented by the peripheral blood is that of a progressive loss of red corpuscles without any marked variation in the size or shape of the cells, and without the presence of nucleated reds. The leucocytes are usually diminished in number, and there is a relative increase in the mononuclear forms with almost complete absence of cells with granular protoplasm. The pathological lesions in our case do not correspond to those found in cases of the Ehrlich type, in fact, instead of a simple aplasia the bone-marrow showed in places a hyperplasia of the mononuclear elements.

Since Ehrlich's case was reported a number of cases have been recorded in which the blood picture was similar. A study of these cases from the pathological side shows that the essential lesions are not in all instances alike. Three main groups may be recognized: (1) Those cases in which the lesions are those of progressive pernicious anæmia. (2) Those cases in which the bone-marrow shows primary (?) aplasia. (3) Those cases in which there is a hyperplasia of the mononuclear elements of the bone-marrow. There is also evidence to show that in one condition which is usually followed by recovery, Barlow's Disease, a blood picture essentially similar to that of aplastic anæmia may be present, and autopsy may show aplastic marrow. This simply indicates that the condition which we clinically term aplastic anæmia is not a pathological entity, but may be due to a variety of causes.

In cases in which the bone-marrow is aplastic throughout there is little difficulty in explaining the blood picture. The same is true of cases of pernicious anæmia with aplasia of the bone-marrow. The actual cause of the aplasia is still obscure. Possibly it is due to conditions similar to those seen in severe infections without leucocytosis, i. e., the causative irritant is of exceptional intensity or the individual power of regeneration is excessively low.

In cases of the character of the one here reported, and the cases of Senator and Wolff[4] seem to be the only similar ones, the blood picture is more difficult of explanation, and the exact nature of the bone-marrow changes is open to discussion.

The explanation of the blood picture in Senator's case does not seem so difficult as in our own, as in his case the bone-marrow was hyperplastic throughout. In this case it might be supposed that the anæmia was due to a crowding out and replacement of the erythroblastic elements such as occurs, according to Dock and Warthin,[5] in chloroma, and presumably in other forms of leukæmia. In our case, however, the shafts of the long bones showed no lymphoid hyperplasia, and it is necessary to assume either that two distinct processes, lymphoid hyperplasia and aplasia, were going on at the same time, or that the hyperplasia, though only partial, caused all the

[4] Wolff: Berliner klinische Wochenschrift. Jahr. 42, No. 2, 1905.

[5] Trans. of the Association of American Physicians, 1904.

changes. The latter seems to us the more probable. One hypothesis which Senator advances seems to explain both the hyperplasia and the anæmia much more satisfactorily than does a mechanical replacement and crowding out. This explanation is, that the lymphoid cells which have undergone hyperplasia represent the parent cells from which should arise both the red corpuscles and the granular leucocytes. It is easily seen that if these cells fail to go through their normal cycle of existence, and instead undergo proliferation unchanged, neither red cells nor granular leucocytes could be produced. Why in our case there should be no regenerative changes in the marrow of the long bones is more difficult to explain unless we assume that when this marrow regenerates the regeneration takes place by the emigration of leucocytes from pre-existing red marrow. Perhaps the same cause which produces the loss of differentiating power in the parent cells also leads to a loss of power to emigrate, though Senator's case does not support this view.

Query as to the exact nature of the bone-marrow hyperplasia in these cases brings up the whole subject of the pathology of leukæmia and allied conditions. Senator regards his case as a pure myelogenous pseudoleukæmia and our case closely resembles his. The relation of such cases to lymphatic leukæmia is still doubtful. There are cases on record in which the blood picture is said to have changed from that of pseudoleukæmia to that of leukæmia, and there are cases of lymphatic leukæmia in which the leucocytes have dropped to normal, or even below normal, before death. Inasmuch as the ordinary lesions of leukæmia were wanting in the internal organs in this case it might seem improper to class it with this disease, though the bone-marrow changes correspond closely to those found in cases of lymphatic leukæmia without enlargement of the lymph nodes. If we follow Warthin's[6] recent classification of the leukæmias, based on the theory that the essential lesion is a neoplasm of the leucoblasts, the case would be classed as a nonchloromatous aleukæmic leucoblastoma, and such we believe to be the most rational interpretation of it. After all the classification of this group of diseases must rest upon the pathological findings, and not upon the clinical picture and the changes in the blood in the peripheral circulation. The mere fact that in one case the proliferated cells gain access to the circulation while in another they do not, may serve as a basis for clinical classification, but does not alter the fact that the underlying pathological condition in both classes of cases is essentially the same.

[6] Trans. of the Association of American Physicians, 1904.

PRELIMINARY COMMUNICATION REGARDING AN IMMUNE BODY CAPABLE OF INHIBITING THE DEVELOPMENT OF CANCER IN MICE (ADENO-CARCINOMA, JENSEN).[1]

By G. H. A. Clowes, Ph. D., *Gratwick Research Laboratory.*

This communication deals with one phase of an investigation which is being carried out at the present time by Dr. H. R. Gaylord and myself, assisted by Mr. F. W. Baeslack.

A considerable number of authentic cases of recovery from cancer in human beings are recorded in the literature but no attempt has apparently been made to test the effect exerted by the serum of such recovered cases upon tumors of like nature in other individuals. We have not up to the present been able to procure human cases of a type suitable for experiments of this nature, but the possession of a series of readily transplanted mice tumors, some of which recovered spontaneously has afforded us an opportunity of making some preliminary investigations regarding the influence exerted by the serum of those mice which have recovered upon rapidly developing tumors in other mice.

In the spring of 1904 Dr. Gaylord visited Copenhagen and received through the courtesy of Professor Jensen of the Veterinarian High School in Copenhagen a couple of white mice inoculated with tumors described by Jensen as adeno-carcinoma (Centralblat f. Bakt. Vol. 34). These mice died shortly before reaching Buffalo but transplantations from one of them were successful, twelve out of twenty-four mice developing tumors in the course of three or four weeks, thus affording ample material for the subsequent inoculation of a large number of normal mice.

We did not in the course of these early experiments observe any marked hereditary tendencies. In some cases an exceptionally large percentage of tumors were obtained on inoculation of the offspring of mice that had themselves exhibited a considerable resistance to inoculation. Great difficulty was at first experienced in transplanting this material to gray mice but in the course of the autumn the inoculation of a batch of sixteen young gray mice (the offspring of non-susceptible parents) resulted in the production of ten rapidly and excessively virulent tumors which, as will be seen later, were of great value in maintaining the tumor series.

Early in July a series of experiments made with a view to determining certain physical and chemical constants was commenced, but received a serious check a couple of months later when the discovery was made that a considerable number of unused small tumors had undergone spontaneous retrogression, the mice having recovered entirely and showing no tendency to fresh development of cancer. At the time at which this incident occurred the number of actively growing tumors was too small to permit of any of them being employed to test the efficiency of the serum of the spontaneously recovered mice immediately after the disappearance of the tumors, but a

[1] Presented to the Jonhs Hopkins Medical Society of Baltimore, January 16, 1905.

month later, the series having been once more established through the successful inoculation of the young gray mice referred to above and of certain other white mice, it was possible to commence work of this nature. A series of experiments was then undertaken making use of both gray and white mice having tumors varying from the size of a pea to that of a large cherry. In every case two mice derived from the same source, inoculated at the same time and having tumors of about the same size, were used for comparison, one receiving a dose of the blood obtained by killing one of the spontaneously recovered mice, the other receiving an equivalent dose of normal mouse blood. A marked effect was exerted by the immune serum on small tumors, three of which about the size of peas disappeared in four or five days, residues consisting almost entirely of connective tissue being all that was to be found on subsequent operation. A larger tumor about the size of a cherry treated in the same manner diminished considerably in size, became harder and remained stationary in its development, was removed successfully by operation and has not recurred in the course of the last month. A microscopic examination of the tumor in question showed a marked increase in connective tissue with destruction of the greater portion of the cancerous epithelium. A still larger tumor was retarded in its development, reduced slightly in size and eventually one-half removed by operation, the remainder being left for further developments. (A considerable amount of blood was lost at the operation, the animal was subsequently bled for other purposes and eventually, the treatment with immune serum having been suspended, the tumor once more developed and formed local metastases.)

Tumors weighing more than three or four grams were not appreciably affected by the serum, but the cachexia from which the mice suffer in the last stages was in all cases noticeably alleviated. The tumors in the control mice referred to above which had received the normal serum were unaffected and developed in the usual manner leading eventually to the death of the animals. The serum of the mice cured of their tumors by the above treatment was found to possess a certain degree of activity, in one case causing the disappearance of a tumor as large as a buckshot in less than two days, but it can scarcely be said to have exhibited as great a degree of activity as did that which was obtained from certain spontaneously recovered mice. The activity of the serum of spontaneously recovered mice varies apparently within very wide limits. Whilst in two cases .2 cc. produced a marked effect on tumors weighing from two to three grams in two or three days, in the majority of cases only smaller tumors were influenced and in four or five of the spontaneously recovered mice no serum activity whatever was to be noted.

Up to the present (January 15) experiments have been carried out on twenty mice. Of those treated with repeated doses of the so-called immune serum one only has failed to show some effect which may be attributed to the serum and all are still living. Of those treated with equivalent doses of normal serum, five are already dead and the remaining mice have tumors exceeding in size those of the mice for which they served as controls.

It must of course be borne in mind that these mice tumors are very irregular in their development some appearing within a fortnight and others as late as five months after inoculation; some developing so rapidly as to reach dimensions almost equal to those of the mice themselves and causing the death of the animal in a fortnight's time, whilst others develop much more slowly not producing a fatal result in less than ten or twelve weeks. With such variations under normal circumstances the greatest precautions must necessarily be observed in drawing conclusions from the above experiments but it must be remembered that at the time at which they were carried out, the tendency to spontaneous recovery was far less than in the previous generation; also that only in one case has a tumor larger than a buckshot been known to recover spontaneously.

Apolant in a communication from Ehrlich's laboratory regarding the influence of radium on mice tumors makes no mention of having tested the serum of cases which had been cured. (Deutsche med. Wochenschr. 24 March, 1904.) Not having radium of sufficient activity at our disposal we have exposed a series of tumor mice to the x-rays and in three cases in which fair sized tumors were cured by this treatment the serum when tested was found to produce no appreciable effect upon other tumors.

A series of test tube experiments carried out to determine the nature of this serum make it appear extremely improbable that it can be classed in the category of cytolysins. In any case it does not exert a more marked hæmolytic effect than does normal serum or the serum of a mouse dying of cancer.

Sections of tumors which have undergone partial spontaneous retrogression show changes in the epithelium closely allied to simple atrophy. The connective tissue stroma of the tumor is greatly increased in amount and if the tumor is not removed for a few days nothing is found but a connective tissue nodule containing isolated masses of degenerating coalescing epithelial cells. The tumors inhibited in growth show about the periphery a marked increase in connective tissue stroma with extensive round-celled infiltration, characteristics which are not to be found to the same extent in the growing tumors. Disintegration of cancer nests associated with atrophy of the epithelium and the formation of coalescent masses of the latter cells characterize those tumors which have been successfully treated as well as those which have recovered spontaneously. Minute masses of connective tissue presenting the characteristics of ordinary organizing connective tissue are frequently all that is to be found a few days after treatment of a small tumor. In general, it may be said that the changes found in the spontaneously cured tumors and in those inhibited or cured with the immune serum, correspond fairly closely to the changes already described by several authors as indications of partial spontaneous recovery from human cancers.

Whilst it is to be hoped that work of a similar nature may eventually lead to the discovery of a means of treating human cancer, it must be borne in mind that the proportion of spontaneous recoveries in mice, which amounted in the course

of our work to 15 or 20 per cent is so far as we know, infinitely greater than the percentage of such recoveries in human beings. Also, whilst the microscopic appearance of the tumor has remained unchanged, it is impossible with the limited data at our disposal to estimate at present the effect which may have been exerted by repeated transplantations of the tumor material from one mouse to another, amounting to at least thirty generations from the first Jensen mouse. In any case it appears probable that a combination of circumstances has in the course of our experiments, led to such a modification of the original conditions as to render it possible for a relatively slight immunizing factor to exert sufficient influence to turn the scale in favor of the normal protective forces of the animal.

The point upon which we would lay special stress is the evidence afforded by the above experiments of the existence of immune forces antagonistic to the development of cancer.

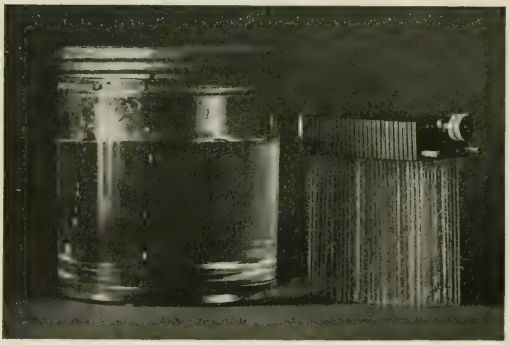
A MULTIPLEX SLIDE-HOLDING DEVICE.

By Edward F. Miller.

(From the Hearst Anatomical Laboratory, University of California.)

Anyone who has had much experience in staining a large number of paraffin sections for class use or research work has been impressed with the enormous waste of time and energy in preparing these specimens. Not only is the process expensive from the view-point of the labor involved, but also on account of the waste of re-agents and alcohols. Of the various mechanisms that have been devised to obviate these difficulties, perhaps the most successful hitherto have been special dishes so constructed as to prevent the slides from rubbing against each other and designed as well to be economical in the quantity of fluid used. While these dishes have solved the problem to some extent, the technician has never been able thus far to handle more than a single slide at once. It has seemed, desirable, therefore, to place on the market a simple device, which I have designed to make it possible to treat a large number of slides bearing paraffine sections at one time and to keep them as well in such a small compass as to minimize the waste of stains, re-agents and alcohols in the process of mounting.

The Multiplex Slide-holding Device consists of a series of perforated vulcanized-rubber plates placed in a holder so that they may be clamped against a metal plate by means of a thumbscrew. The device is exceedingly simple, is not acted upon by any of the re-agents used either in the simple or complex methods of staining, is easily cleaned, and, when ordinary precautions are taken, is practically indestructible. From an inspection of the illustration, the method of using the apparatus is at once self-evident, although there are worth noting one or two points concerning its use which may save the technician some time and trouble. The holder has a carrying capacity of 26 slides, which should be placed between the vulcanized-rubber plates and then clamped securely by means of the thumbscrew. Care should be taken to place the side of the slide bearing the sections towards the part of the holder marked "Front," for not infrequently after the preparation is complete it is difficult to determine which side of the slide the sections are on. This simple precaution prevents the possibility of sections being rubbed or injured. It is, of course, obvious that this point is of the utmost importance in the preparation of serial sections, where the loss of a single one may destroy the value of the entire series. It is not advisable to clamp the slides between the vulcanized plates back to back in order to increase the capacity from 26 to 52, for capillary attraction draws the fluid between the slides whence it is difficult to extract it by the ordinary processes of diffusion and consequently stains or water are carried to the higher alcohols or even to xylol, thus preventing the subsequent clearing of the sections. If it is necessary to handle more than 26 sections at once, it is advisable to use two



or more holders. In the ordinary methods of preparation, that is to say, with the commoner nuclear stains and contrasts, the holder with 26 slides may be taken directly through the stains as an ordinary section without any precautions being taken; but in the more complex special methods of staining, the time element, particularly in tissues fixed by different methods, is often of importance. Under these circumstances it is advisable to carry a test slide through the stain in order to determine the exact time required to get the desired result. After this is done the holder with the large number of slides is treated exactly like the control. In this way 27 slides may be stained in the time ordinarily consumed in preparing two.

The results, furthermore, are absolutely equal, as the unequal intensity of stain that is sometimes embarrassing in careful work is thereby obviated. In my experience, it is not necessary to leave the slide-holder laden to its maximum capacity in the re-agents longer than one would leave a single slide. This is particularly true if it is moved about in order to bring fresh fluid in contact with the sections. Care should be taken not to allow either stains or the lower alcohols to come in contact with the slide-holder. This is easily done if the level of the fluid in the baths is adjusted so as to keep it 4 or 5 mm. below the slide-holder. When the staining and subsequent dehydration is almost complete, the slide-holder is inverted in absolute alcohol in order to remove any possible water that may have come in contact with the holder. After removal from the absolute alcohol the thumbscrew is loosened and again inverted in the xylol bath. As soon as the clearing is complete, the slides may be removed directly from the bath one by one and mounted; the portion of the holder marked "front" determining, of course, the side of the slide to which the sections adhere. As the slide-holder is taken from one bath and placed in another, it is always better to drain the slides by touching the free ends to filter-paper, blotter or some other absorbent medium. This precaution, of course, prevents the waste of re-agents. It may be mentioned that the prolonged action of xylol softens the vulcanized rubber; but the entire holder can be immersed in xylol repeatedly for a time sufficient to clear any set of sections without injuring it in the slightest. The construction is so simple that it can be very easily taken apart for the purpose of cleaning and drying, a precaution which will naturally prolong the life of the instrument.

Two types of jars have been found serviceable in our experience to hold the stains and re-agents, one a battery jar with a glass lid and the other a round dish with a metallic screw-top. The battery jar has the advantage of using a small amount of fluid, which is particularly desirable when the more expensive stains are used. It is, indeed, possible to economize still more by immersing the slides in a deep Stender dish, which will hold a dozen or more of the slides. Although the round jars with screw-tops take a greater volume of liquid, I have found that owing to the tight screw-tops, in the end, they are quite as economical as the square dishes owing to the prevention of evaporation. The same bath consequently may be used for a greater length of time than in the case of the battery jar.

The instrument is manufactured by the Spencer Lens Company of Buffalo, New York, and is sold by them. In case the vulcanized rubber deteriorates it may be purchased separately. To sum up the advantages of this apparatus, we may say that:

First: 26 slides bearing paraffine sections may be stained and mounted with but a slightly greater expenditure of time than is consumed in staining and mounting a single section.

Second: There is a great saving in the quantity of re-agents used when the slide-holder is employed.

Third: There is no danger of injuring the sections. The entire series can be mounted without the loss of a single section.

Fourth: The staining of the entire set is absolutely uniform, a result impossible to obtain by the old method.

Fifth: The apparatus is so constructed as to be, with ordinary care, almost indestructible.

Sixth: By the use of this holder it may be possible to give to classes in microscopic anatomy sections stained by the more complex methods owing to the economy of time and re-agents.

DR. HEINRICH OR HENRY KEERL, OF BALTIMORE, THE "HESSIAN SURGEON."

By Eugene F. Cordell, M. D.

We have all read of the famous Hessian troops who fought against us in the Revolutionary War. The name has always had a very bad odor among us, for why should these Germans leave their own homes to fight the battles of a nation and a war in which they had not the least interest. We forget that those were the days of absolutism, when men, as Frederick the Great said, were esteemed little more than cattle. There is ample evidence that many of these men sympathised with patriots who were fighting for their freedom from foreign oppression and would have exchanged sides if they had dared.

It is not generally known perhaps, that one of these Hessians, a distinguished surgeon, settled in this city, and after a long, honorable and successful career died, leaving many prominent and influential descendants here.

Dr. Keerl was descended from a Bavarian family, of the higher class, which could trace its lineage back to the beginning of the sixteenth century. He was born in the town of Mainbernheim, thirteen miles from Würzburg, in the year 1755. He was the only child of his parents who survived, two brothers having died in infancy. Early losing his parents, he was educated by a wealthy uncle, a widower without children, whose wealth according to expectation he was to inherit. He adopted the profession of medicine, completing his studies at the University of Göttingen, then sharing with Halle the supremacy of the German universities. Meanwhile his uncle married again, thus dissipating his prospects of affluence. About this time the American war broke out and the British Government hired the soldiers of some of the petty German princes to aid them in subduing their rebellious colonies. By his uncle's influence, Dr. Keerl obtained a commission as surgeon in one of these "Hessian Regiments" (as they were called), commanded by Colonel von Rall. He left Germany with his command more in a spirit of adventure than from any definite purpose of life, and expecting to re-

turn at the end of his term of service. But "Der Mensch denkt's, Gott lenkt's," and it was destined that he should not see his native land again.

The employment of the troops of the Rhenish principalities by George III is an episode of the American war of great interest and I have already alluded to it at length in a paper read before the German Historical Society entitled, "A Memoir of John Peter Ahl, Surgeon's Mate in the Continental Army." Dr. Ahl also probably came over with the Hessians, at any rate he was in the British service. Early in the war he espoused the cause of the patriots, served them faithfully and was severely wounded while defending some of their sick and wounded from an attack of Tarleton's dragoons at White Plains on the Hudson. After the war he settled in Baltimore and died here in the same year as Dr. Keerl.

The treaty between George III and the Landgrave of Hesse Cassel, dated January 15, 1776, calls for 12,000 men of the troops of Hesse to be employd in the former's service, consisting of four battalions of grenadiers of four companies each, fifteen battalions of infantry of five companies each, and two companies of chasseurs. Part of this force was to be ready to march February 15, 1776, and the remainder four weeks later, if possible. These troops formed a part of the army of General Howe operating against Washington from New York and were under General Heister, who was recalled after the Trenton affair. Over 4000 Brunswickers under General Riedesel were assigned to the army operating from the direction of Canada under Burgoyne and surrendered with that general at Saratoga. The exact number of German troops hired by Great Britain was 16,900.

The brigade of von Rall, consisting of his own, von Knyphausen's and von Losberg's regiments, had covered itself with glory in the campaign of 1776, taking conspicuous part in the battle of White Plains and in the storming of Fort Washington on the Hudson. As a reward for this distinguished gallantry, to it was assigned the post of honor at the close of the campaign by being stationed on the farthest outpost—that directly in front of Washington's army. It occupied the best winter quarters at Trenton.

It is well known how von Rall, elated by his successes, and sharing the opinion, general throughout the British army, that Washington was crushed and the war virtually at an end, neglected the commonest dictates of prudence. Although within but a few miles of a hostile force and although warned, he refused to believe that he was in any danger or that precautions against attack were called for. Well, suffice it to say, that after a Christmas spent in drinking and festivity, von Rall and his men retired to their heavy slumbers to be aroused early the following morning by Washington and his men who had crossed the Delaware and surprised them. Von Rall, hearing the firing, rushed from his quarters and bravely attempted to form his command, but was wounded at the beginning of the action. It is said that he fell into the arms of Dr. Keerl and expired shortly after, entrusting to his surgeon for his wife his watch and sword. The Germans endeavored to retreat but were cut off and captured, suffering a loss of 17 killed, 78 wounded, and 868 prisoners.

So depressed had become the spirits of the Americans that they would not believe that the Hessians had been beaten, and Washington had to march his prisoners through the streets of Philadelphia in order to convince his countrymen. The prisoners were marched to the interior of Pennsylvania for safety. The officers petitioned to go with them but were not allowed to do so; they were sent on the 6th of January, 1777, to Baltimore, where they were paroled. Dr. Keerl spent some time traveling through the country, no doubt with a view to permanent location. At one time he and a friend visited the Carolinas and, according to family tradition, "were solicited to remain and marry among the rich widows whose husbands had been killed in the war." But having formed agreeable acquaintances and finding a favorable opening in Baltimore, he settled finally here about the year 1782, and devoted himself with industry to his profession, meeting with the success which his assiduity and professional acquirements entitled him to. His residence was at 17 West German Street. His experience in the service and the reputation he had acquired as a surgeon were of great advantage to him and brought him forward especially in the line of surgery. He rapidly acquired practice and friends among the best people in the town. In connection with his profession he had a drug store, which was situated on Baltimore Street near Sharp. In the *Maryland Journal* of August, 1789, he advertises the sale of medicines and instruments at the "Sign of the Golden Swan, upper end of Market Street, near Congress Hall." He also kept for sale glassware of all kinds.

From the time of his settlement in Baltimore, Dr. Keerl seems to have had an uneventful life, moving as Horace says,

> "With soul serene amid the nooks
> And silent by-ways of a blameless life."

He early became a member of the Medical and Chirurgical Faculty of Maryland. That he was a Lutheran seems probable from the name "Heinrich Keerl," appearing in the list of contributors to the building of the Gay Street Church, finished in 1808. [See Dr. Scheib's article on the Early Lutheran Church in Baltimore, Transactions of the German Historical Society, Vol. I.] He invested his earnings in real estate, and at his death, which occurred on the 6th of July, 1827, he left to his family a very considerable fortune, which was divided equitably by will among his heirs.

He was twice married; first in early life to Anna Maria, daughter of Jacob Myers, a prominent merchant of Baltimore and one of the founders of the German Presbyterian Church which stood for many years at the corner of Baltimore and Front Streets. His second wife was Margaret Kandel, of Frederick, Md. By his first marriage he left four sons, viz.: John C., Samuel, George H., and Joshua. The first-named was educated in Germany, receiving from his professors there the highest testimonials to his character and attainments. He began life as a merchant, took part in the battles of Bladensburg and North Point, and retired from business in middle

life. Samuel was a director in the Firemen's Insurance Company and for a long period president of the first Baltimore Hose Company, composed entirely of leading young men of Baltimore, and especially of representatives of the principal Quaker families. He also participated in the War of 1812. Gorge H. was of the firm of Henry Keerl & Sons, wholesale druggists, Baltimore Street near Howard, and carried on this business up to his death; he left six children. George H. and Joshua were partners and also married sisters, but the latter died early and left no issue; the other two brothers never married. One of the daughters of George H. married Dr. Robert Atkinson, of Baltimore.

By his second marriage, Dr. Keerl left three children, of whom William pursued medical study in Paris, married Ellen Douglass, of Maryland, a daughter of Colonel Douglass, of the Revolution, and moved to Charlestown, W. Va., where his descendants now reside. One of his sons was killed in the Confederate Army. Charles, the second son, settled in Hagerstown, and Amelia married Dr. Robert Fulton, of Baltimore, and left two sons, one of them, Dr. Henry Keerl Fulton, a graduate of the University of Maryland, who lived in Washington. Dr. Keerl's second wife died in 1866.

Of the German branch of Dr. Keerl's family, a distinguished representative recently resided at Schloss Liebersteen, near Augsberg, Germany, and other descendants and members were not many years ago residing at Nuremberg, and heartily welcomed their American relatives who visited them there. Before his death Dr. Keerl had a very beautiful monument erected over the grave of his mother.

The descendants of Dr. Keerl in Baltimore have in their possession an oil painting of him said to be by one of the Peales; also an old German bible, his sword and letters and pictures of Mainbernheim and of the University of Göttingen, where he was educated. At one time they also had his pair of pistols, but they have been lost. The portrait represents a robust, vigorous man of forty-five or fifty years, with full, clean-shaven, oval face and ruddy complexion; a handsome face, full of intelligence and character.

The following obituary notice of Dr. Keerl appeared in the Baltimore papers at the time of his death: "On Monday evening, 16th inst., Dr. Henry Keerl, in the 73d year of his age. Dr. Keerl was one of the oldest inhabitants of Baltimore, and the respect due to his memory may be safely left to the decision of his fellow-citizens. Plain and unoffending in manners, conscientious and just in his dealings, benevolent and liberal on all proper occasions of public or private charity, he enjoyed and deserved the entire confidence, esteem and good will of all to whom he was known. At that solemn crisis when the world was fast fading from his view, he contemplated the close of his earthly career with calmness and resignation. To him who can look back on a long life spent in the habitual practice of piety and virtue, death is disarmed of all its terrors." [*Baltimore Gazette and Daily Advertiser*, July 18, 1827.]

Dr. Keerl's will is dated November 8, 1823. He leaves his wife, Margaret Keerl, $1200 per annum for life out of the rents of his two warehouses or stores on the south side of Baltimore Street, one occupied by George H. and Joshua S. Keerl, druggists; the other by Samuel Keerl, as a dry goods store; if these rents be not sufficient, the amount is to be made up from his ground rents. He also gives her his house and lot in German Street, as long as she remains a widow. To his sons William and Charles he gives $10,000 each. To his daughter Amelia Henrietta he leaves the interest arising from 66 shares of stock in the Bank of the United States and 12 shares of stock in the Bank of Baltimore, the said shares to go to her in trust at the age of 18. Also to this same daughter a negro girl who is to have her freedom at the age of 44, his piano-forte and one-half of his household and kitchen furniture. He also leaves to his wife one-half of his household and kitchen furniture and two negroes who are to be free at the age of 44. He authorizes his executors to lease his unimproved ground for 99 years, renewable forever. After the above dispositions, the rest of the estate is to be divided into seven equal parts, one of which is to go to each of his sons, viz.: John C., John Samuel, George H., Joshua S., William, Charles F., and to his daughter Amelia Henrietta. He explains that he has already previously given to each of his four oldest sons $10,000, and has also allowed to his son George H. $4000 in addition for his conduct of the business theretofore pursued by him. Finally, he appoints his friend Charles Bohn and his son George H. as his executors.

We learn from this will that Dr. Keerl had accumulated what was a large fortune for his times, and it seems to have been due entirely to his industry, good judgment and business capacity.

STUDIES IN TYPHOID FEVER.

SERIES I-II-III.

The papers on Typhoid Fever, edited by Professor William Osler, M. D., and printed in Volumes IV, V and VIII of the Johns Hopkins Hospital Reports, have been brought together and bound in cloth.

The volume includes thirty-five papers by Doctors Osler, Thayer, Hewetson, Blumer, Flexner, Reed, Parsons, Finney, Cushing, Lyon, Mitchell, Hamburger, Dobbin, Camac, Gwyn, Emerson and Young. It contains 776 pages, large octavo, with illustrations.

The price is $5.00 per copy. Address The Johns Hopkins Press, Baltimore, Maryland.

THE BACILLUS AEROGENES CAPSULATUS IN PUERPERAL INFECTION.

By Herbert M. Little, M. D.

Resident Obstetrician, The Johns Hopkins Hospital.

(*From the Obstetrical Department of the Johns Hopkins Hospital and University.*)

In 1897, Dobbin reported from this clinic the isolation of *B. aerogenes capsulatus* from a case of physometra, and suggested that this organism was the true etiological factor concerned in its production. This observation has since been abundantly confirmed by other investigators, though the rôle of the gas bacillus as an infecting agent has received much more attention from pathologists than from obstetricians.

Apart from Dobbin's original case and one which he observed subsequently, no one in America or England has recorded the isolation of this bacillus during the course of puerperal fever. Such observations, however, have been made both in France and Germany, and as in both countries the organism is described under varying names, it may be well to consider briefly the various bacteria which have been described as original but which are nevertheless undoubtedly identical with the bacillus of Welch and Nuttall.

B. aerogenes capsulatus (Bacterium Welchii, Migula, 1900), better known in America as the "gas bacillus," was first described by Welch and Nuttall in 1892. Dr. Welch has briefly given its characteristics as follows: "A rather coarse, non-motile, anaerobic bacillus; stains by Gram; grows on all of the ordinary culture media under anaerobic conditions, best at body temperature but also at room temperature; liquefies gelatine slowly; forms spores constantly according to the race and culture medium; and is capable of generating gas, not only by fermentation of sugars but also from proteids."

Capsules are usually readily demonstrable with the usual stains, particularly when the bacilli are grown in milk or obtained directly from the tissues of an inoculated animal.

Milk is probably the most satisfactory culture medium as the reaction is very striking. The milk becomes acidified and coagulated, then partially digested, giving a "worm-eaten" appearance to the clot. For absolute identification, this reaction may be supplemented by the other characteristic test suggested by Welch; namely, the production of gas in the tissues of a rabbit killed within a few moments after the injection of an emulsion of the organism into its ear vein. This last test, which Dr. Welch considers the most important of all for the identification of the bacillus, we have applied in every instance with positive results, and we were also able to obtain the organism from the heart's blood of the animal.

The Vibrion Septique.—This organism, or complex of organisms, was discovered by Pasteur in a class of puerperal cases which appeared to him to have a peculiarly fatal course. Unfortunately, he was never able to cultivate it alone, but of recent years it has been generally believed that the bacillus of malignant œdema, isolated by Koch, represents it in pure culture. There is, however, reasonable ground for doubting whether this view is really correct, since Pasteur's vibrion was frequently present in cases of puerperal infection and was widely distributed in nature, being invariably present in the intestinal canal and in cases of putrid gangrene. It was motile in the absence of oxygen but lost its power of motion when exposed to the air. The bacillus of malignant œdema, on the other hand, is far less widely distributed, is rarely isolated from the human intestine, and, so far as I have been able to ascertain, plays a very limited part in the production of puerperal infection. Moreover, it differs from the gas bacillus in being motile and decolorizing when stained by Gram's method; but this latter test was unknown to Pasteur. In short, *B. aerogenes capsulatus* seems to conform very closely to the description of the vibrion septique, and the isolation of an identical organism from a large number of cases of criminal abortion—the only class of cases now exposed to the same danger of infection as all cases in Pasteur's time—renders it highly probable that the organism in question represented an impure culture of the gas bacillus.

In 1880, Doleris, who was a pupil of Pasteur, divided the bacteria giving rise to puerperal fever, into micrococci and "Bactéries Cylindriques Septiques,"—the latter a new name for the vibrion septique. Eighteen years later, in reporting the autopsy findings in a case of infection following the removal of the placenta by a midwife, he noted that the body was distended with gas and that three organisms were present, streptococcus and colon bacillus, which were obtained in pure culture, and also the *vibrion septique,* which he could not isolate.

Menereul, likewise, reported a case of crepitating gangrene which he ascribed to infection with the vibrion septique, although the results of his cultures and inoculations make it reasonably certain that he had to deal with the gas bacillus. Indeed, a study of the French literature upon the subject, from 1880 until the present time, gives a practically unbroken chain of evidence in favor of the identity of Pasteur's organism and *B. aerogenes capsulatus.*

Bacillus Phlegmones Emphysematosæ.—In 1893, Fraenkel described as the cause of gaseous phlegmons, the organism to which he gave the above name. The same year Ernst isolated a similar organism at an autopsy upon a case of infected abortion, but both bacteria were believed to differ in some degree from the original gas bacillus. Goebel in 1895 insisted upon the identity of the three; and although as far back as 1899 Fraenkel admitted this to be true, his organism is the only one widely known in Germany.

Bacillus Perfringens.—This bacillus was isolated from cases of otitis, mastoiditis, pulmonary gangrene, appendicitis, Bartholinitis and pelvic abscess, and was described by Veillon and Zubert in 1897. One year later the same investigators admitted that it was identical with Fraenkel's bacillus, but in France, it nevertheless retains the name given by them.

Bacillus Emphysematis Vaginæ.—Lindenthal in 1897 described this organism as the cause of gas cysts of the vagina and isolated it in two of six cases examined during pregnancy. In 1899, working with Hitschmann, he admitted its identity with *B. aerogenes capsulatus* as well as with Fraenkel's bacillus. His original communication is of interest as an evidence of the peculiar distribution of the gas bacillus.

The Granulobacillus Saccharobutyricus Immobilis Liquefaciens.—This bacterium was isolated by Schattenfroh and Grassberger from a great many samples of milk, ground water, etc.; and there would appear to be but little doubt as to its identity with the various bacilli noted above.

Bacillus Aerogenes Aerophilis Agilis.—In 1902, Uffenheimer isolated this bacillus at an autopsy upon a case of puerperal infection; and his note, "Exemplare ihre Beweglichkeit verloren," together with the admitted mixed character of the infection, would, apart from some imperfections of his technique, as pointed out by Westenhoffer, suggest that he was dealing with an impure culture of the gas bacillus.

Only one other organism is perhaps worthy of mention in this connection—the *B. septique aerobie* of Legros and Lecène. This seems to be identical with what Dr. Welch calls the aerobic form of the gas bacillus, and is practically interesting from the fact that it was so named to accentuate its points of similarity with, and dissimilarity from, the vibrion septique.

The cultural characteristics and pathological properties of *B. aerogenes capsulatus* are well known; but many are not aware of the extent of its distribution. It has been found regularly in the fæces of human beings, as well as of dogs, cats, and swine, also in those of rabbits, rats, guinea-pigs, mice, chickens, and cows, and likewise in the excreta of flies found hovering about dead bodies. It is frequently found in garden earth, but rarely in street dust; occasionally it may be isolated from the dust of hospital wards and from scrapings of the human skin. Its presence in the uterus in cases of infection is not surprising.

According to Dr. Welch its introduction into the pregnant or puerperal uterus may give rise to one or more of the following conditions:

I. Emphysema of the fœtus.
II. Puerperal endometritis.
III. Physometra.
IV. Emphysema of uterine wall.
V. Gas sepsis.

Being chiefly concerned, in this article, with puerperal endometritis, we shall slightly alter this order and consider the second subdivision last.

Emphysema of the Fœtus.—Knowledge of the pathology of the condition dates from Dobbin's observations in 1897. In his case, infection of the fœtus occurred by way of the placental circulation. Krönig and Menge have shown that the liquor amnii may become infected prior to the rupture of the membranes (l. c., p. 90), and in three cases reported by them (p. 167) the infection of the fœtus was undoubtedly due to the swallowing of infected amniotic fluid.

Physometra or Tympania Uteri.—Formerly it was held that this condition could be produced by the aspiration of ordinary air into the uterus, but it is now universally recognized as being bacterial in origin. Gebhard in 1893 analyzed six cases and found in all a bacillus which he identified as Bacillus coli. In four cases it occurred in pure culture, while in two others it was associated with the streptococcus.

Chiari, Hitschmann, and Lindenthal have shown that Bacillus coli is capable of producing gas only in the tissues of diabetics. Moreover, the clinical and experimental work of the latter observers, supplemented by that of Halban, has shown that even this is very exceptional, and has served to confirm Dobbin's suggestion that the gas bacillus is the usual cause.

Emphysema of the uterine wall is usually associated with tympania uteri and has a like causation. It is of interest, as the condition frequently found at autopsies on cases dying as a result of puerperal infection, and was the lesion present in the case from which Ernst's bacillus was obtained.

Gas sepsis is probably the most important of the five subdivisions. Though cases showing evidence of general infection with the gas bacillus are not infrequently seen at autopsy, it is often difficult to decide whether the infection occurred during life or postmortem. Thus, in thirteen cases collected by Dr. Welch the evidence of ante-mortem invasion of the tissues seemed conclusive in but seven, including those of Dobbin, Ernst, Halban, and Krönig and Menge above referred to, and two others reported by Wood, and Graham, Steward and Baldwin, respectively. In none of these cases was the bacillus isolated from the blood during life; and but five cases have been reported in which this has been accomplished, all of which terminated fatally. Thus, Gwynn repeatedly cultivated the bacillus from the blood in a case of chorea, and Cole, and Norris from cases of infection following trauma; while the two remaining instances occurred in connection with puerperal infection, and are recorded by Fraenkel and Lenharz. Fraenkel's case was reported with practically no detail, while in Lenharz's the patient died from a general infection following an abortion at the second month. The vagina had been tamponed. There were marked pyrexia, jaundice, and air-hunger; later the patient became irrational. At autopsy, gas was present in the heart, and bacilli were found in sections from all the organs. There was no note of general emphysema.

In Case 9, which is reported in detail in the latter part of this article, the infection of the rabbit, the presence of bacilli in the smear preparations, and the distribution of the organisms in the microscopical sections of the tissues, leave little

or no room for doubt that the bacillus was present in the blood some days prior to death.

Puerperal endometritis is second in importance only to gas sepsis, and must be considered as a possible forerunner of that condition. Apart from cases ascribed to *Bacillus perfringens* by Mouchotte and Jeannin, no examples of such infection have been reported since Dobbin's paper.

Mouchotte, examining the uterine lochia from eighteen cases of abortion occurring between the second and the fifth months, isolated *Bacillus perfringens* in thirteen cases or 72%. In no instance was it present alone, being usually associated with streptococci, staphylococci, or *Bacillus coli.* Three of the thirteen patients died and one came to autopsy, at which there was no note of the presence of gas in the organs. Jeannin, likewise, made cultures from the fœtal surface of the placenta in five cases of delayed labor and obtained *Bacillus perfringens* in four. In his cases there was high fever (103°-104° F.) lasting from four to eleven days after delivery. The same observer has recorded the bacteriological findings in twenty-one cases of puerperal infection, *Bacillus coli* being noted in eighteen and *Bacillus perfringens* in twelve (57%).

The clinical character of the latter group of cases is interesting. In four, premature rupture of the membranes occurred, and in six, portions of the placenta or membranes were retained after delivery. The fever was noted as early as the first and as late as the eighth day, and invariably reached 103°-104°. Two cases died on the twenty-fifth and the forty-fifth days, respectively. There was no note of the condition found at autopsy.

In addition, Jeannin examined eighteen cases of incomplete abortion with subsequent infection, and isolated *Bacillus perfringens* twelve times. Streptococci were equally frequent and the *Bacillus coli* was present in fifteen cases. Two of the patients died, but there was no autopsy. Clinically, this group of cases is also of interest. In one instance there was no fever; in three the temperature dropped from 104° to normal immediately after cleaning out the uterus; while in two others a sudden drop to normal was noted after slight preliminary rise, and none of the six had fever subsequently. A seventh case had a slight temperature on the second day, and two other rises on the fourth and sixth days, respectively; though the cultures taken with these rises suggest infection at the time of operation. Thus, in all his cases, the tendency was for the fever to fall abruptly upon cleansing the uterus. Jeannin has also reported three cases of physometra in which *Bacillus perfringens* was isolated. Two of these cases died and came to autopsy but there is no note of general infection, nor of the presence of gas in the tissues.

Finally, Rist and Mouchotte reported three cases of infection following abortion, in two of which they were able to obtain *Bacillus perfringens* from the uterine cavity. Streptococci and staphylococci were also present, and, in one instance, other anaerobes. The fever was alarmingly high in both cases, but recovery followed in each. These observers suggest the identity of *Bacillus perfringens* with Fraenkel's bacillus and the vibrion septique.

Our experience with the gas bacillus comprises some fifteen cases in the Obstetrical Department of the Johns Hopkins Hospital, in only ten of which was the bacillus identified with absolute certainty. These, including Dobbin's two cases, are given in detail below.

Bacillus aerogenes capsulatus may gain access to the uterine cavity in one of two ways. The first, and by far the more usual, is its introduction by means of the examining finger or by instruments. By reason of its almost invariable presence in the fæces of human beings, this is particularly liable to occur in spontaneous labor when the perineal and vulvar regions are insufficiently cleansed, as well as in operative cases even in spite of this care. In the second place, the organisms may occasionally be present in the circulating blood, by which they are carried to the uterus, and then be cultivated from the lochial discharge. It is noteworthy in this connection, that in both of our cases which terminated fatally, intestinal ulcers were found at autopsy.

The passage of the gas bacillus into the circulation by way of typhoid ulcers is not merely a hypothetical supposition, as Hitschmann and Lindenthal have reported the case of a boy, æt. 8, in whom a general infection could apparently be traced directly to such lesions.

The presence of bacteria similar to or identical with *B. aerogenes capsulatus* has not as yet been noted by any of the investigators of the organisms present in the normal vagina, and the two cases in which they were found by Lindenthal in gas cysts must be considered quite exceptional.

It is worthy of note, that of our ten cases of infection, seven followed operative procedures, and an eighth, a self-induced abortion. All of these had been repeatedly examined. In one case, however, which entered the hospital profoundly infected, the patient stated that she had not been examined vaginally. The organisms cultivated from this patient were obligate anaerobes, and this was one of the cases in which intestinal ulcers were found at autopsy.

Once within the uterus, the character of the reaction produced will probably vary with the facilities for growth and development afforded by circumstances. Krönig has stated that anaerobes cannot develop in the uterus in the presence of oxygen, and it would seem that the anaerobic growth is favored by such procedures as packing the vagina. In cases where the infection is mixed, it is doubtful whether free drainage would preclude the growth of anaerobes; since, as Kedrowski has shown, aerobes in their development not only absorb a certain amount of oxygen, but also give off some substance favoring the growth of anaerobes. We, ourselves, have noted that, even with free access of air, the gas bacillus developed fairly profusely in milk when associated with the staphylococcus aureus.

Symbiosis, moreover, would not only appear to favor the growth, but also to enhance the virulence of the organism. Thus, Achalme, as early as 1880, increased the virulence of streptococci by associating anaerobes with them. Roger, Novy

and Penzo have also shown that the association of *B. proteus* or *B. prodigiosus* will markedly increase the virulence of the bacillus of malignant œdema; while Besson has noted the same in reference to the vibrion septique. The last-named observer even goes so far as to say that the vibrion septique is harmless in healthy tissues unless in association with other bacteria.

On the other hand, the work of Dr. Welch, confirmed by Fraenkel, and more recently by Kamen, leaves no doubt as to the ability of the gas bacillus to induce by itself a typical inflammatory reaction; but it is interesting to note that in only two of our cases (one of which was a case of mastitis) was the organism found alone. In a third case (B. L., Case 7), the cultures take after the febrile rise showed only the gas bacillus, but a previous culture had shown in addition the presence of streptococci.

It is the custom in the Obstetrical Department of the Johns Hopkins Hospital to examine the uterine contents bacteriologically in every case in which the temperature reaches 102° during the puerperium, and to take cultures after the conclusion of the third stage of labor whenever the patient enters with a temperature, or has been subjected to attempts at delivery by persons not connected with the department. Likewise in all cases of incomplete abortion, especially if of a criminal character, cultures are taken before the patient is examined vaginally.

In every instance 2-4 cc. of the uterine contents are secured by means of a lochial tube, and from this inoculations are made upon various culture media,—plain agar, hydrocele agar, blood serum, milk, and bouillon. Routine anaerobic inoculations are made by mixing the lochia with glucose agar which has been freshly sterilized or boiled, then cooled rapidly to 40°. After inoculation, the agar is allowed to solidify and its free surface is then covered with a layer of paraffin or agar. In the majority of cases, however, two sets of tubes are inoculated, one of which is incubated in an atmosphere of hydrogen.

Should the gas bacillus be present, there is usually no difficulty in recognizing it in coverslip preparations made directly from the uterine contents, particularly when stained by Gram's method. When associated with other organisms, its isolation in pure culture may offer some difficulty. Fraenkel suggested that this could be effected by killing off the other microorganisms, taking advantage of the fact that the bacillus in question offers considerable resistance to heat—Pasteurization. For this purpose the inoculated tubes are placed in a water bath and heated to 65° C. for three to five minutes, after which they are removed and cooled. It has been repeatedly demonstrated that the gas bacillus will survive this treatment, (according to Fraenkel it will withstand 70° C. for three minutes), while its more usual associates will for the most part be destroyed.

When the organism has been isolated in pure culture, we have, as noted above, invariably proven its identity by obtaining a characteristic reaction after its inoculation into a rabbit.

If for no other reason, the recognition of the presence of the gas bacillus is important in relation to that large group of cases known as "Sapræmia;" "to produce which," according to one American authority, "germs of putrefaction—saprophytes—must gain access to the uterus after labor." The diagnosis in this class of fevers is usually not based upon bacteriological examination, but merely upon the benign clinical course of the case, and the fallacy of this method is shown by the fact that Bumm was able to demonstrate streptococci in a number of cases presenting the supposedly characteristic clinical features. Moreover, the observations of Jeannin as well as the bacteriological findings in our cases (Cases 4 and 6) bear out the contention of Bumm and Williams, that no case should be diagnosed as Sapræmia without a bacteriological examination.

Doleris says that all organisms found in saprophytic infections have been found in the vagina. As *B. aerogenes capsulatus* is not an inhabitant of the vagina, and as it would appear neither advisable nor justifiable to classify it with the ordinary putrefactive bacteria, the possibility of its giving rise to autoinfection or Sapræmia is very remote. This being the case, it is probably always introduced from without, and just as in streptococcic infection, the physician should be held responsible for its introduction, unless satisfactory proof to the contrary can be adduced.

The ideal treatment in these cases of infection is, of course, prophylactic, and this can best be attained by careful aseptic technique during labor. In the Johns Hopkins Hospital the routine is as follows: A rectal enema is given during the first stage of labor, and the patient is prepared for vaginal examination by first clipping close the vulvar hair, then scrubbing with green soap and water, followed by sponging with 95% alcohol; finally, a towel soaked in a 1-2000 bichloride solution is applied, and left in position until the examination—a minimum of three minutes. In all operative cases the vulva and perineum are shaved and cleansed by the permanganate-oxalic-acid method in addition to the above. The hands are disinfected as for major operations. No douches of any kind are given. If no details of this technique are omitted, the results will be good. Unfortunately, in emergency cases it is often necessary to operate without the preliminary enema, and the introduction of the hand during operations such as version may unavoidably carry up intestinal bacteria into the vagina and uterus. But even if this occurs the bacteria may cause no trouble, provided the third stage be carefully conducted and no portions of the placenta or membranes be retained.

Should fever ensue, the first requisite is an accurate diagnosis. This is important more from the standpoint of prognosis than of treatment, as the latter, no matter what the infecting agent, will, in general, be along three lines: (1) removal of necrotic material offering a medium for growth of organisms, (2) establishment of free drainage from

the uterus, and (3) stimulation of the natural resistance of the patient. The finger should be used in removing débris, as the curette, however carefully manipulated, will undoubtedly interfere with the attempt at local reaction on the part of maternal tissues and may open up sinuses and dislodge thrombi. A large douche (4 liters) of hot salt solution (110° F.) will also aid in cleansing the cavity. So-called antiseptic douches will accomplish little that the salt solution will not, while the danger of poisoning from absorption should not be overlooked. If the cervix is sufficiently patulous to admit two fingers, as good drainage will be obtained by leaving it alone as by introducing gauze. To aid resistance, the patients are well fed and when necessary strychnia and alcohol are given; but the greatest emphasis is placed on the necessity for large quantities of fluids either taken by mouth or injected into the rectum.

The greatest danger to be feared is the passage of the organisms from the uterus into the circulating blood. While patients with streptococcus septicæmia not infrequently recover, all known instances of gas sepsis have ended fatally. If the infection be grave and definitely localized in the uterus, hysterectomy is justifiable, but theoretically, only when the infection is on the point of becoming generalized. The difficulty in establishing this definite moment is obvious, and the operation, as in our Case 9, may completely fail in accomplishing its purpose.

Following is a synopsis of the cases in which we have demonstrated the presence of the gas bacillus. Two of them had been noted previously in the articles of Drs. Welch and Dobbin, but are here incorporated for the sake of completeness.

It is not contended, nor is it intended to imply that *B. aerogenes capsulatus* was, in each instance, the determining factor in the causation of the fever. The varying effects of such infection have been shown above, and even when typical gas production is absent, the possibility of the organism in question in influencing the virulence of others with which it may be associated, must be continually borne in mind.

Case I.—*Generally contracted pelvis; dystocia; frequent examinations by midwife; gas noted in vaginal discharge; basiotripsy; death.*

P. A., (O. O. S. No. 56.) (Dobbin's first case.)

"A Bohemian woman with a generally contracted pelvis had been in labor some three to four days under the care of a midwife. When she came into our hands, the head of a macerated child was found firmly engaged in the superior strait, the uterus being in a state of tetanic contraction. A fœtid, dark-colored discharge, which contained many gas bubbles, was escaping from the vagina with a crackling sound. Delivery was effected by means of Tarnier's basiotribe. The mother was profoundly infected and died next day. Within a few hours after death her body had nearly doubled its original size, as a result of development of gas in the subcutaneous tissues. Similar changes were observed in the fœtus and placenta, and we were able to demonstrate the presence of the gas bacillus in the tissues of both, as well as in the uterine lochia. No autopsy was allowed."

Case II.—*Generally contracted rachitic pelvis; dystocia; frequent examinations and attempts to deliver; rise of temperature during labor; prolapse of cord; perforation and extraction of child; recovery.*

M S., (H. No. 316.) 1-para, white, was admitted to the hospital in labor. An outside physician had made several vaginal examinations and had attempted delivery with forceps. The following are extracts from the note on admission:—"Small, slightly-built woman, facies expressive of suffering, pinched and drawn; superficial examination suggests rachitis; breasts large, nipples prominent, colostrum; heart and lungs negative; abdomen enlarged to size of full term pregnancy, fundus two fingers' breadth below ensiform; there is no contraction ring, though the uterus is apparently tetanically contracted; the round ligaments converge upwards. An accurate diagnosis of the presentation and position is impossible, though the occiput is directed downward and to the left side. No fœtal heart heard. The pelvic measurements are Sp. 23.5, Cr. 23.5, Tr. 28, D. B. 16.5 cm."

The results of vaginal examination were as follows: "Marked œdema of soft parts; forceps abrasions; cervix fully dilated, cord prolapsed, not pulsating. The head is movable at the superior strait in L. O. I. T., the sagittal suture being only about 1.5 cm. from the symphysis pubis; there is a marked caput succedaneum. The diagonal conjugate measures 9.5 cm. and the antero-posterior and transverse diameters of the outlet are 8 cm. and 7.5 cm., respectively. At this time, the patient's temperature was 101°, her pulse 108 and her respiration 22 per minute."

The head was perforated and the child extracted with the cranioclast. It was 46 cm. long and weighed 1850 gms. without the brain. There were no macroscopic evidences of infection, but a uterine culture was taken immediately after the completion of the third stage of labor. The day after delivery the patient's temperature reached 103°, and the following day a second culture was taken and a douche given. The fever persisted for seven days but the woman left the hospital in excellent condition.

Bacteriological Report, M. S., Fever Case 64.

Culture I.

Smears show a few cocci and a number of large bacilli with rounded ends.

Cultures show:—*Streptococcus pyogenes, Staphylococcus albus.*

Culture II.

Smears show bacilli similar to those previously seen. Capsules can be demonstrated.

Cultures show:—*Streptococcus pyogenes, Staphylococcus albus, Bacillus coli, Bacillus aerogenes capsulatus.*

Case III.—*Generally contracted pelvis; dystocia; frequent vaginal examinations; rise of temperature during labor; craniotomy; recovery.*

A. T., (O. O. S. No. 762), a black primipara, was seen in consultation outside the hospital. She had been in labor for two days and had been repeatedly examined. She was dull and listless. Temperature 101°, pulse 120. Her uterus was tetanically contracted upon a large child; no fœtal heart heard. The pelvis measured Sp. 22.5, Cr. 24, Tr. 28, D. B. 18. Vaginal examination: Outlet relaxed, vagina hot and dry, cervix fully dilated, membranes ruptured; head at brim, in L. O. I. A., not engaged; diagonal conjugate 10 cm. A marked caput succedaneum had formed and palpation of this elicited gaseous crepitation. The forceps was applied ineffectually and craniotomy was resorted to, the placenta being subsequently removed manually. Cultures were made from the liquor amnii, and from the lochia on the first day of the puerperium.

At autopsy upon the child there was abundant evidence of general infection with the gas bacillus.

Bacteriological Report, A. T., Fever Case 102.

Source of cultures:—(a) Liquor amnii, (b) Uterine lochia.

Smears show micrococci and bacilli.

Cultures show:—*Streptococcus pyogenes, Bacillus coli, B. aerogenes capsulatus.*

This patient's temperature chart is unusual in that but slight rises in temperature are noted, in no instance above 100°. This may possibly be explained by the fact that the temperature was taken but twice daily, and at irregular intervals.

Case IV.—*Inevitable abortion; vaginal pack; marked rise in temperature subsequent to labor. Sapræmia (?).*

M. W., (H. No. 1145), a white multipara, entered the hospital April 10, 1902, with a history of irregular bleeding for two weeks, which became alarmingly free two days previous to entry. She had menstruated last October 21, 1901.

The fundus uteri was one finger's breadth above the umbilicus, the child lying in L. S. I. A. No fœtal heart heard. Temporizing measures were employed, but the bleeding continued, and as there was no evidence of life on the part of the fœtus, it was decided to induce labor. The vagina was accordingly packed with sterile gauze which stimulated the uterus to contract, and at 5 a. m., April 12, the patient spontaneously expelled a dead fœtus (6 mos.). The same day about 6 p. m., subsequent to the expulsion of some large clots covered with decidua, the temperature rose to 103°, and the pulse to 108. There were no subjective symptoms and the temperature became normal within 48 hours.

Bacteriological Report, M. W., Fever Case 184.

Source of cultures:—*Uterine lochia.*

Smears show coarse bacilli staining by Gram's method.

Cultures show:—*B. aerogenes capsulatus.*

Case V.—*Precipitate labor; hæmorrhage; collapse; submammary infusion; mastitis.*

E. W., (O. O. S. No. 619), a white primipara, had a precipitate labor resulting in a bad perineal laceration. The placenta was retained, but as it was desired to repair the perineal tear at once, Crede's method of expression was employed. The patient subsequently collapsed, and was infused with 2000 cc. of sterilized normal salt solution prepared from tap water. The following day her temperature rose to 102°, but almost immediately fell to normal. On the fifth day it again rose, reaching 103.4°, with evidence of local inflammation in one breast. This was incised and drained, after which the puerperium was uneventful.

Bacteriological Report, E. W., Fever Case 84.

Source of Culture:—Pus from breast abscess.

Smears } show *B. aerogenes capsulatus.*
Cultures }

This case has been included with a view of showing the great danger of infection in all procedures such as douches and irrigations where the asepsis is not absolute, and as evidence of the fact recently insisted upon by Kamen, that the gas bacillus may operate alone in producing local inflammation, particularly if superimposed upon an injury.

Case VI.—*Normal pelvis and pregnancy; self-induced abortion; infection; removal of infected ovum; recovery.*

O. H., (H. No. 1738), a white multipara, was admitted to the hospital March 30, 1904. She had menstruated last in December, 1903, and one week previous to admission (i. e., March 22, 1904), knowing herself to be pregnant, had introduced a bougie into her cervix for the purpose of inducing an abortion. This was attended by slight bleeding, which persisted until entry into the hospital. The night prior to her admission (March 29) she had had a slight chill and vomited a good deal. The day of admission she had five slight chills, and entered with a temperature of 102.7° and a pulse of 136.

From external examination little could be made out except slight tenderness above the symphysis pubis, but as there was a foul-smelling discharge from the vagina, preparations were made to remove the infected ovum. The patient was anæsthetized and prepared for operation in the usual manner. A culture was taken from thhe uterine cavity, after which the cervix was dilated to admit the finger. A considerable amount of foul-smelling tissue was removed, and the uterine cavity was thoroughly washed out with normal salt solution. Within twelve hours the temperature fell to normal, where it remained till the 13th day, when it rose following a vaginal examination, but fell to normal again almost immediately.

The tissue removed from the uterus was preserved and examined microscopically.

O. H., Current work No. 689. Microscopic examination.

The specimen apparently consists of the entire ovum. The amnion and chorionic membrane are completely necrotic, as well as the villi immediately surrounding the latter. The decidua is well-marked, and shows but slight development of Nitabuch's layer; between it and the amnion are chorionic villi in all stages of degeneration, some perfectly normal, others completely degenerate. There are no blood-vessels; most of the intervillous spaces are filled with blood, though here and there it is distinctly coagulated. Sections stained by the Gram-Weigert method show myriads of thick bacilli of varying lengths, and also cocci. Diagnosis: Infected abortion.

Bacteriological Report, O. H., Case 249.

Source of Culture:—Uterine cavity before operation.

Smears show chiefly large coarse bacilli, often in pairs and frequently intracellular. They retain Gram's stain.

Culture shows:—*Micrococcus aureus, Micrococcus albus, B. aerogenes capsulatus.*

It is noteworthy that in addition to its development in all the cultures grown anaerobically, the gas bacillus was also demonstrable in the milk grown aerobically probably owing to its association with staphylococci.

Case VII.—*Normal pelvis and pregnancy; prolonged labor; dystocia; Champetier de Ribes Balloon; version and extraction; post partum hæmorrhage; vaginal pack; puerperal infection: recovery.*

B. L., H. No. 1597, a white multipara æt. 41, was admitted to the hospital on October 31, 1903. She had been pregnant ten times before, five of her children being still-born and three others living for only a few minutes after birth. One child had presented by the breech, but apart from this and one forceps operation, her labors had been normal. She invariably lost much blood after the labor, particularly after the last, when "the after-birth came before the child." Following this confinement she was in bed four weeks with fever, and since that time menstruation has been painful. Last menstruation February 15, 1903. Examination showed the presence of a cystic goitre, a rapid pulse, and slight œdema of the lower limbs; apart from this her condition was normal.

Pains began 10 p. m., November 29, but in spite of the fact that they became hard and frequent, the cervix failed to dilate. On December 2, at 8.30 p. m., a Champetier de Ribes bag was introduced into the cervix, and was expelled four hours later, when the cervix was found three-fourths dilated. During the night the patient's temperature rose to 101.6°, but almost immediately fell to normal. After the expulsion of the bag the pains gradually ceased and the patient slept till morning, when, in the complete absence of pains, it was decided to complete the dilatation of the cervix manually and deliver the child by version. The version was readily accomplished, but owing to the large size of the child's head, great difficulty was experienced in extraction, and though the fœtal heart continued to beat for several minutes after delivery, the child could not be resuscitated.

The patient lost 1000 cc. of blood during the third stage, and examination showed a slight perineal tear and also a bilateral laceration of the cervix. The former was repaired immediately,

but as the uterus contracted firmly after the expulsion of the placenta and the bleeding abated, suturing the cervix was considered inadvisable. A uterine culture was taken immediately after the third stage. Four hours after the completion of the operation the bleeding still continued and as it was evidently from the cervix, it was thought that it might be controlled by a vaginal pack, which was accordingly carefully introduced. The patient's pulse had risen to 156 per minute, but following the introduction of the pack and the administration of stimulants, marked improvement occurred. The pack was removed some eighteen hours later (9 a. m., December 4).

On the morning of the third day (the day following the removal of the pack), a second uterine culture was taken. The cervix was far back, its lumen practically occluded. When its anterior lip was drawn forward with a tenaculum, a large amount of foul-smelling brown fluid escaped from the uterus, but there was no evidence of the presence of gas. Following the culture, the temperature rose to 101.4° but fell again to normal, rising to 104° the next day at 4 p. m., falling during the night to 97°, but reaching 103.6° at 8 a. m. With both these rises there were chills, but the patient's general condition remained good and the physical examination was negative save that the fundus uteri was soft and high, and the lochia rather foul.

The day of the first rise (4th day) the hæmoglobin was 45%; the leucocyte count, 20,200.

After the second rise (5th day, 8 a. m.) a third uterine culture was taken and a douche of 2 litres of salt solution was given. A blood culture was also taken.

The fever continued till the 9th day, varying from 100° to 103°, but the patient gradually improved, and left the hospital the 22d day in excellent condition.

Bacteriological Report, B. L., Fever Case 235.

Source of culture:—Uterine lochia.

(a) Immediately after labor.

Smears, negative.

Cultures, negative.

(b) Morning of third day.

Smears show numerous thick bacilli with rounded ends, stained by Gram's method; no cocci seen.

Cultures show:—*Streptococcus pyogenes*, *B. aerogenes capsulatus*.

(c) Morning of 5th day.

Smears show as in "(b)."

Cultures:—*Aerobic, negative. Anaerobic, B. aerogenes capsulatus.* Blood culture, 5th day, negative.

The streptococci were evidently few in number, and accordingly narrowly escaped being overlooked. Low has pointed out that in large numbers of cases where colon bacilli alone are demonstrable, the primary invader is the streptococcus, which later outgrown, cannot be obtained in cultures.

Case VIII.—*Incomplete abortion; curettage; septicæmia with anaerobic organism; thrombosis; death.*

M. F., (H. No. 1702), a colored multipara, entered the hospital February 20, 1904. She had been perfectly well up to February 12, having menstruated last in November, 1903. On the day noted above she began to bleed, without any apparent cause, and during the night passed a mass of some sort per vaginam. Since then she had bled at irregular intervals. She denied any internal examinations or manipulations. She was a sparely-built colored woman, eyes sunken, mucous membranes pale, tongue coated, temperature 102.7°, pulse 130, respiration 30. No other abnormality was noted on physical examination. She was prepared for operation in the usual manner and a uterine culture was taken before an internal examination was made. The uterus was then curetted and douched with a large quantity of salt solution. After the operation the temperature rose to 104.3° and remained above 101.7° till the morning of the third day, when it became subnormal, rapidly rising again to 106°. This same day thrombosis of the left saphenous vein was noted, though there was practically no œdema of the extremity. The leucocyte count was 28,000. From this time on, the temperature remained persistently elevated, frequently reaching 105° and occasionally 107°.

Blood cultures taken on the 8th and 11th days were positive, as well as a urine culture the 15th day. Jaundice was noted on the 6th day, but never became marked. Patient died the 18th day.

Anatomical diagnosis, M. F., Autopsy 2260: "Abortion, clean uterine cavity; thrombosis of vena cava, left common iliac, femoral and saphenous veins, partial thrombosis of right iliac vein. Embolic abscesses in the lung. Cloudy swelling of liver and kidney. General anæmia. Hæmorrhagic ulcers of rectum. Acute splenic tumor. Infarct of spleen. Jaundice. Oidio-mycosis of œsophagus. No formation of gas in the organs.

Examination of material removed from the uterus by curettage 11 days post abortum. (Current work No. 677.)

"The stroma is much denser than usual, and is infiltrated with round cells and a few leucocytes. Scattered through the tissue are a few areas which stain brightly with eosin, some of which are apparently fibrinous in character, while in others distinct remnants of decidual cells can be found. Examination with the high power shows at the margins of portions of the endometrium, but particularly in the blood surrounding, numerous cocci, and occasionally large thick bacilli. The cocci are usually in groups, but short chains are also to be seen. The bacilli occur in an isolated manner and in no case can more than two be found in the same field."

Bacteriological Report, M. F., Fever Case 239.

A. Source of culture:—Uterine cavity.

Smears show micrococci in chains, also coarse bacilli, occasionally in chains. Both forms retain Gram's stain. The bacilli are occasionally seen within leucocytes.

Culture:—Aerobic plates and tubes absolutely negative.

Anaerobic tubes show:—(I) *B. aerogenes capsulatus*, (II) a streptococcus.

B. Blood.

Source of culture:—Blood from med.-basilic vein.

Culture I, made on the 8th day.

Ten tubes of various forms of agar were inoculated for the purpose of making plate cultures, but as by accident there were but 9 plates, 9 tubes were poured, and in one the agar was allowed to solidify. After incubation there was absolutely no growth on any of the plates but in the bottom of the solid tube, several colonies were seen. These proved to be a micrococcus growing in chains and similar to the one isolated from the uterus.

Blood culture No. II, made on 11th day.

Bearing in mind the previous result, ten tubes were inoculated as before and when pouring them into Petri dishes, about 2 cc. of the medium was retained in the tubes, which were rolled and cooled in the manner described by Esmarch. Five plates and the same number of tubes, selected indiscriminately, were incubated in the usual manner, and the others, in an atmosphere of hydrogen. None of the former showed any growth after 5 days, while numerous colonies developed upon those incubated anaerobically. These consisted of micrococci growing in chains, apparently identical with those previously obtained.

C. Urine.

Source of culture:—Catheterized urine.

No. I:—Made on the 15th day (contaminated).

No. II:—Second culture obtained within five minutes after death of patient showed in all media streptococci and an unidentified bacillus. The cocci were noted in both aerobic and anaerobic

tubes, possibly developing in the former as a result of the symbiosis.

In all instances the organism was apparently identical with that first obtained from the uterine cavity, and had the following characteristics: Micrococcus, invariably paired, more frequently in chains of ten to twelve elements. Retains Gram's stain (1.2.5 min.). Grown on agar mixed with blood frequently shows a distinct hæmolytic ring. Capsules not demonstrated. No spores, no motility.

Anaerobic growth was as follows:

Milk.—Acidity, no coagulation.

Glucose-bouillon.—Slight sediment.

Glucose-agar.—Fine pin-point raised pale gray colonies.

Blood serum.—Similar growth.

Hydrocele agar.—Similar growth, more profuse.

Transfers were made to various media in attempt to obtain aerobic growth. There was a slight growth on one hydrocele agar tube and one or two colonies on blood serum. The remaining tubes showed no growth and transfers could not be obtained from the two noted as positive.

At autopsy the same organism was obtained from the thrombus and by gradually reducing the percentage of hydrogen in which it was grown, aerobic cultures were finally obtained. These, however, died out in two or three days. The presence of a capsule was also suggested. So far as I am able to learn, this is the first instance recorded in which an anaerobic organism other than the gas bacillus has been obtained from the blood during life. The case is also of interest from the fact that in spite of the almost complete occlusion of the veins of the extremity there was practically no œdema and the swelling was only appreciated after more careful comparative measurements.

Case IX.—*Febricula during pregnancy; normal labor; puerperal fever. Isolation of Bacillus aerogenes capsulatus from the uterus; blood culture negative; hysterectomy; isolation of Bacillus aerogenes capsulatus (?) and Bacillus typhosus from the circulating blood; death; lesions of typhoid fever; gas bacilli and typhoid bacilli in cultures at autopsy, and in sections from organs.*

L. S., (H. No. 1597), æt. 19, black, 1-para, married. Was first seen in the dispensary January 9, 1903. Her previous pregnancy and labor had been normal and her condition at that time was excellent. The pelvis measured Sp. 24.5, Cr. 26, Troch. 30, D. B. 18, D. C. 11.75.

She was admitted to the hospital January 18. Her condition then, apart from pregnancy, was quite normal: Temperature 97.6°, pulse 92, respiration 24. On the third day following her admission (January 20) she complained of some headache, and had a temperature of 100.4°. For nine days the temperature ran an irregular course, elevated in the afternoon, normal in the morning, only once reaching 102°. In the afternoons, she occasionally complained of headache and pain in the back of the neck, but these invariably disappeared by the following morning. Typhoid fever was thought of, but there was complete absence of definite symptoms and physical signs; moreover, as she had a doubtful history of syphilitic infection, she was put upon antisyphilitic treatment and apparently improved under it, the fever gradually subsiding, so that she appeared perfectly well on January 30.

Labor pains began early in the morning of February 2, and she was delivered spontaneously at 5 p. m. The child and placenta were normal. On account of the fever before labor, a uterine culture was taken immediately after the completion of the third stage.

On February 4 (third day post partum) there was no visible growth in the tubes and a second culture was taken, in the smears from which, long chains of Gram-staining bacilli were found Two hours after this culture, the patient's temperature rose to 104°. A blood culture was taken on February 5, and on February 6 (fifth day) a third culture from the uterus, followed by a douche of salt solution. Part of the material obtained was inoculated into a rabbit which was shortly afterwards killed and incubated.

On February 7 (sixth day post partum) as the temperature was still markedly elevated, the rabbit having shown the definite lesions induced by Bacillus aerogenes capsulatus and the inoculations of various media with uterine lochia confirming this test, while no growth had occurred in the blood culture, supra-vaginal hysterectomy was done by Dr. Williams.

Following the operation the temperature fell almost immediately to 100.5°, but rose the following morning to 105.6° and ranged between 102° and 106° until death, 16 days later. The pulse was very rapid, never below 130 per minute, sometimes reaching 180. The patient was frequently irrational, and passed fæces and urine involuntarily; she could, however, answer intelligently till within 24 hours of her death. She complained of no pain, but towards the end dyspnœa became marked.

Treatment consisted in general stimulation with strychnia and digitalin, aided by infusions of large amounts of normal salt solution.

Clinical Bacteriology.

Uterine culture "A" at completion of labor, February 2.

Smears negative.

Aerobic and anaerobic inoculations upon various media.

Examination of same, four days later.

Aerobic cultures:—Negative.

Anaerobic cultures:—No growth in bouillon or milk; abundant growth of long, coarse bacilli retaining Gram's stain, in the condensation water of the blood serum tubes: Capsule stain positive, and spore-bearing forms seen. This organism inoculated into a rabbit produced lesions typical of those caused by Bacillus aerogenes capsulatus, the organism being cultivated from the heart's blood.

Uterine culture "B," third day after labor, February 4.

Smears showed Gram-staining thick bacilli, singly and in chains.

Aerobic and anaerobic inoculations:—Negative.

Uterine culture "C," fifth day after labor, February 6.

Smears show many thick bacilli. May occur singly and in chains, retain Gram's stain and resemble Bacillus aerogenes capsulatus.

Aerobic and anaerobic inoculations were made as before, and at the same time 2 cc. of the lochia was diluted with an equal volume of sterile bouillon and the mixture injected into the ear vein of a rabbit, which was killed five minutes later, and placed in the incubator for eight hours.

At autopsy typical gas bacillus lesions were present and the organisms were obtained on smears and cultures from the heart's blood.

Blood culture "A," February 4.

Aerobic and anaerobic inoculations negative after four days in thermostat.

Blood culture "B," February 10.

Owing to the poor quality of the circulation and the smallness of the superficial veins, only about 2 cc. of blood was obtained. The entire quantity was immediately injected into the ear vein of a rabbit, which was subsequently killed, and placed in incubator. The following morning the animal was markedly distended and Bacillus aerogenes capsulatus was obtained from its heart's blood in cover slip preparation and cultures.

On the advice of Dr. Welch, the above result was not considered absolutely conclusive, as the organism had not been grown in artificial media, and therefore the possibility of contamination from the intestine of the rabbit had to be considered.

Blood culture "C," February 15.

Blood obtained from right-median cephalic vein and a large number of inoculations made. At the same time 15 cc. of blood was collected under weak bichloride solution, but no gas bubbles were observed. Upon centrifugalization with weak acetic acid, a number of bacilli, similar to those previously described, were found in the sediment, as well as a few others, differing slightly in morphology.

After 48 hours there was no growth except in the milk, and in one hydrocele agar tube, the former appeared slightly acidified, while a few non-Gram-staining bacilli were found in the condensation water of the latter. The tubes were re-incubated anaerobically, but no change was noted.

February 23 secondary inoculations were made from the milk flasks and showed an aerobic bacillus, which by its cultural and agglutinative reaction was proved to be Bacillus typhosus.

At the autopsy upon the patient (No. 2252, February 23, 1904), Dr. Bunting made the following anatomical diagnosis:—Typhoid fever; operation (amputation of uterus), infected abdominal wound; œdema and atalectasis of lungs; cloudy swelling of liver and kidneys; œdema and swelling of the pancreas; multiple abscesses of the kidney; acute splenic tumor; early arteriosclerosis; healing ulcers in small intestine.

Bacteriological examination by Dr. W. W. Ford gave the following results:

Bacillus typhosus in heart, blood, and spleen.

Bacillus aerogenes capsulatus in abdominal wound, spleen, kidney, and ureteral abscess.

Micrococcus aureus in ureteral abscess.

Microscopic examination of heart, lungs, liver, pancreas, and spleen were without special interest, as far as our case is concerned. On the other hand bacteria were demonstrated in the kidneys, mesenteric lymph glands, intestine, and appendix, as follows:

Kidney.—Capsular surface is regular, convoluted tubules dilated; epithelium is low, granular, and ragged; the lumina show the granular precipitate of the so-called "colloid-droplets." A few hyaline casts are found. The glomeruli are congested, their capsular spaces dilated and show granular precipitates. The interstitial tissue is œdematous, but is apparently not increased in amount. In one portion of the section there are several distinct abscesses which show cellular detritus and pus cells, chiefly of the polymorphonuclear type. In the periphery of the abscess, however, there are mononuclear cells which are actively phagocytic for other nucleated elements. There are groups of *short, coarse bacilli, occurring in pairs, found in the abscess; also much coarser bacilli occurring chiefly at one focus.*

Mesenteric Lymph Glands.—Show the sinuses crowded with large mononuclear cells, many of which are phagocytic for lymphocytes. The glands also show œdema and scattered areas in which the cells are necrotic. There is apparently also hyperplasia of the lymphoid elements. The glands themselves and especially their capsules, with the intervening connective tissue, *show very many coarse, long bacilli, often in pairs or short chains.*

Intestine.—Peyer's patches show increase in the epithelioid elements and small mononuclear cells, with superficial necrosis, and also scattered areas of necrosis in the depth of the swollen patches. In these areas there is fragmentation of nuclei, degeneration of the cells and infiltration. The epithelioid cells are phagocytic.

The Appendix.—Shows in the lumen a necrotic slough. Necrosis also extends into the wall of the appendix to the muscularis at one point; the wall is here infiltrated with leucocytes. *In the slough are a few coarse bacilli, similar to those already described, also smaller bacilli.*

Examination of the puerperal uterus removed by supra-vaginal hysterectomy:—The organ weighs 515 grammes and measures 13 x 13 x 6.5 cm. Externally there is no abnormality. On opening its cavity, which measures 9 x 5.5 cm., a dark tenacious clot is disclosed 5 x 4 x 2 cm. On removing this, the placental site is found in the upper left quadrant of the posterior wall, it measuring 6 x 4.5 cm. and covered with black protruding thrombi.

Microscopic examination on the greater part of the clot consists of fibrin, though included in it here and there are areas of degenerated tissue containing spaces with apparently hyaline walls. Large numbers of bacilli are readily demonstrable, both in the fibrin and the degenerated tissue.

Sections from the placental site show internally a thick layer of fibrin with very few cells in its meshes. Between this and the muscularis is a thin layer of degenerated tissue, more or less infiltrated with blood, and richly supplied with blood-vessels, chiefly venous in character. Where the tissue is well preserved, it is made up of spindle-shaped cells with fusiform nuclei; scattered through it are large numbers of irregularly shaped cells with deeply staining nuclei. *There is no trace of inflammatory reaction.* Protruding into this tissue, but chiefly in the innermost layers of the muscularis, are numerous thrombosed vessels. The muscularis itself presents a normal appearance.

In some of the veins, but particularly in the necrotic tissue corresponding to the endometrium, *many large tolerably thick bacilli can be seen. These stain by Gram's method, but can be seen even in specimens stained with hæmatoxylin and eosin.*

Case No. X. *Rise in temperature during labor; manual dilatation of cervix and extraction of child; puerperal infection; parotitis; recovery.*

B. R., (O. O. S. No. 2170), æt. 25, 2 para. Pelvis normal. Was first seen by Out-patient Department, 8 p. m., April 20. At that time her cervix readily admitted two fingers, but at midnight, in spite of good pains, there was little further dilatation. Patient slept until morning. At 2 p. m., April 21, there had been little advance, but as the patient's temperature was 100.4°, her pulse 105, and the fœtal heart between 160 and 170 per minute, the cervix was dilated by Harris' method and the child extracted. The field of operation had been contaminated by fæces and a douche of hot normal salt solution was given after the completion of the labor. The temperature after labor was 100.6°, and the following day it rose to 102.2°. Its maximum, 103.5°, was reached on the fifth day; but from 103° on the sixth day, it fell to normal on the seventh day, and remained around 100° until the thirteenth day.

Swelling of the parotids was noted the day after operation, but was thought to be due to holding up of the lower jaw during the administration of the anæsthetic. Later, it was learned that a next-door neighbor had mumps, and that a member of the patient's family had had the same disease two weeks previously. A uterine culture was taken and a douche given on the third day, and on the fourth day a blood culture was taken.

While it is quite possible that the primary trouble may have been the parotitis, the presence of marked subinvolution of the uterus noted at examination on the tenth day, makes the bacteriological findings at least of interest.

Fever Records No. 241, B. R., O. O. S. No. 2170, April 23, 1904.

Smears show diplococci and two forms of bacilli, one short, the other large and coarse. All of the bacilli and some of the cocci retain Gram's stain.

Culture.—Gonococcus (I). Diplococcus retaining Gram's stain. Strepto-bacillus aerogenes capsulatus.

Blood cultures taken on the fourth day were negative.

Since the completion of the article two more cases have come under our observation.

I. R. S., H. No. 1886, æt. 41, white, married, aborted on August 17, 1904, when 3½ months pregnant. For seven days her condition was excellent, but on August 24 she had a severe hæmorrhage, to control which an outside physician packed the uterus with iodoform gauze. She was advised to enter the hospital, which she did on August 25.

On admission her temperature was 100° and her pulse 120. Large iodoform gauze packs were removed from the vagina and uterine cavity. A uterine culture was taken, some small fragments of the ovum removed with the finger, and a large douche of hot salt solution was given.

B. coli and *B. aerogenes capsulatus* were grown from the lochia thus obtained, but the patient made an uninterrupted recovery.

II. M. S., a white multipara, entered the hospital July 29, 1904, with a history of having had chills and fever during the day, accompanied by slight bleeding from the uterus. She denied having attempted to induce abortion, but her statement was later proven to be false.

On admission a purulent discharge was noted escaping from the cervix uteri. A uterine culture was taken and the infected ovum removed manually.

She developed pyæmia with panophthalmitis of the right eye and abscesses in the left arm, the abdominal wall, and in the left broad ligament. The eye was removed, the abscesses opened and drained, and the patient made a good recovery.

B. aerogenes capsulatus was associated with streptococci in the original culture, and streptococci were obtained from the patient's blood and from the pus in each of the abscesses.

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PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

January 16, 1904.

A Case of Arterio Venous Aneurism. Dr. Osler.

Dr. Osler showed a patient exhibiting this condition. The man—now 31 years of age—had, in his eleventh year, received a knife-wound just above the right knee. This was soon followed by swelling of the calf of the leg and a little later pulsation was noticed along the femoral artery with the development of a swelling in that region. The patient's health had remained good and he was exceptionally vigorous except for some disability in the right lower limb and for attacks of hemorrhage from varicose veins in the lower leg. Along the outer thigh reaching from the lower ribs to the foot, ran huge, tortuous varicose veins, and the whole right leg was enlarged. Thrombi were palpable in the veins, some of them organized and a few probably calcified. There was a pulsating swelling in Scarpa's space and along the femoral artery. Over this a thrill was felt most intensely about the middle of the thigh. In the abdomen was another pulsating tumor 8 inches across and occupying most of the hypogastrium and right iliac fossa. The pulsation here, too, was expansible in character and over it a thrill could be feebly felt. The abdominal tumor was thought by Dr. Osler to be a large venous sinus associated with the enormous venous dilatation above a traumatic arterio-venous aneurism. Its origin was, however, not perfectly clear, and, so far as he knew, there were no other cases like this one in the literature.

The Immunization of Mice to Cancer. Dr. G. H. A. Clowes.

Dr. Clowes made a preliminary report of recent work on this subject done by him at the Gratwick Laboratory, at Buffalo, in conjunction with Dr. Gaylord. The work started from the study of two mice infected with cancer brought to this country from Professor Jensen of Copenhagen. These animals—which were suffering from subcutaneous carcinoma simplex—died before reaching Buffalo; but inoculations from their tumors, though unsuccessful in the first and second experimental series, finally "took" in a large percentage of the descendants of these inoculated animals (hereditary predisposition?) and the investigators then had cancer experimentally produced on which to work. For the inoculations the tumor material was macerated in twice its weight of sodium chloride and injected subcutaneously. A tumor appeared locally (on the average in about 40% of selected cases), the animal grew cachectic, the blood count fell and the growth became, in a few months, nearly as large as the experimental animal. During the course of the work the

cancer material became attenuated and a certain number of animals with small tumors recovered spontaneously. It was from these recovered mice that immunizing serum was obtained for subsequent experimentation. A series of mice were inoculated with the cancer; half of this number then received a dose (.2 ccm.) of immunizing serum and the other half were kept as controls. This experiment was tried on animals with small, with medium, and with large tumors. In almost every case the difference between the history of the immunized mice and the "controls" was quite marked. In the former small tumors disappeared in about five days, larger tumors diminished to ½ their original size; in the latter, the disease took its usual progress. All the control animals are now dead; all the immunized animals (with the exception of one, dead from infection) are still alive. Later corroboratory experiments, while not quite so satisfactory as the earlier ones, gave in a general way always the same results. Tumors larger than a small cherry were never cured but treatment reduced their size, and rendered them more easily operable. Mice cured by serum immunization had sera capable of further curing, or at least counteracting, the disease. The sera of animals whose tumors had been improved by X-ray treatment were studied but they proved not to be protective. The protecting body of this immunizing serum was not a cytolysin, possessed no particular hemolytic activity and precipitive tests all gave negative results. Its protecting activity was not great and a large dose was necessary. The hope for the application of these results to human cancer lay, of course, in obtaining a case of spontaneously cured (or possibly even improving) cancer and then testing the serum of this patient for protective or curative powers.

Pathological Changes. Dr. Welch.

Dr. Welch discussed the microscopical features of the specimens showed by Dr. Clowes. The tumor produced in the mice was, he said, of the solid or simplex type, without acini and made up of polymorphous cells. The stroma was well developed and the connective tissue quite cellular. In the immunized animals the microscopical picture showed a striking change. In the larger tumors retrogressive metamorphosis was shown by necrosis of many cells at the center by diminution in size of both protoplasm and nuclei of cells still preserved at the edge. In the smaller tumors it was almost impossible to tell that a carcinoma had ever been present, the picture being almost that of an inflammatory granuloma with multinuclear giant cells, necrotic center and vascular connective tissue shell. The observation of Drs. Clowes and Gaylord was, he said, a new and most important one. It offered at least a ray of hope for the treatment of human carcinoma; and while there was, as Dr. Clowes had said, a mathematical possibility that in the mice subsequently treated with serum, the cancer inoculation had led only to the development of an inflammatory new growth while in all the other cases it had produced true cancer and that the results had, therefore, been purely accidental he felt this chance to be almost infinitesimal and the experiments practically conclusive within their own limits. It was extremely improbable that the serum of any animal would have the slightest effect on any human being; a spontaneously cured human being would have to provide the serum.

Apparatus for the Treatment of Fracture of the Femur. Dr. Theodore Dunham.

This apparatus was described by Dr. Dunham who devised it 10 years ago and has been using it successfully ever since. It consisted of a plaster spica of the hip, connected with a plaster bandage of the lower leg by two long metal plates incorporated in the two plaster dressings and fastened together by seizing. In applying the apparatus the plaster bandages were first put on and the metal plates incorporated. Extension was then made in the required direction and the two metal plates lashed together. Coaptation splints might be added for older children but were not indicated for young infants in whom the thigh might be put up at right angles, giving the natural position for nursing. The apparatus gave a constant extension, was simple and easily applied, did not necessitate keeping the patient in bed, did not interfere with the routine of life, allowed the thigh to be frequently examined without removing the dressing and had given excellent results. It was necessary to reapply the seizing at intervals in order to take up slack and keep extension perfect. Size and muscularity made the treatment unsatisfactory in adults.

Treatment of Esophageal Stricture.

Dr. Dunham also demonstrated a method of treatment of "impassable" stricture. A silk thread was passed into an ordinary drinking tube and its loose end allowed to float in a glass of water. The water was then sucked from the glass by the patient through the tube and the silk thread was in this washed down the esophagus. Its lower end could then be caught through a gastrostomy wound and the stricture sawed by the method of Abbé. If regurgitation occurred or the patient resisted with his tongue, the thread could be passed through a rubber tube, inserted into the nostril, and could then be washed down by pouring water into an attached funnel. The lower end of the thread could then be caught through a gastrostomy and the upper end fished out from the pharynx. An instrument for cutting strictures was also shown consisting of a guide bougie on which was locked an olivary-tipped dilator. Through the olive ran a cord, the two ends of which were brought out through the patient's mouth. The filiform guided the dilator, the stricture being thus put on the stretch by the olive and sawed by the string. This allowed further dilation and was followed by further sawing.

A wire and spindle dilator was also shown provided with rubber-protecting tubes for portions of the esophagus both above and below the stricture; and demonstrations of the use of the thread method were given on an apparatus constructed to represent esophageal stricture. Dr. Finney said that the great difficulty in these cases was in once getting something through and that Dr. Dunham had made an important con-

tribution to the solution of this problem. He himself had modified Abbé's method by simply tying knots in the cord and after passing these through fastening larger and larger bits of gauze for the purpose of dilatation.

Peri Pancreatic Abscess. Dr. Thayer.

The case reported by Dr. Thayer was of a woman, aged 51, who had been taken, in June, with epigastric pain and jaundice. From this she recovered but shortly afterward had an attack of very severe abdominal pain accompanied by jaundice, fever, nausea, and vomiting. Fever was intermittent in character and there were night sweats. She complained of a "sore pain" in the left abdomen where there was a slight prominence, especially above the iliac crest. A deep mass could be felt which did not reach to the perinephric region. Two weeks later, however, it had reached the loin and the kidney. Operation was performed by Dr. Finney, a peripancreatic abscess with fat necrosis being found and drained. Four similar cases had been seen at the Johns Hopkins Hospital characterized by abdominal pain (the onset being, in some cases, exceedingly severe), usually jaundice, fever, sweats, sometimes chills and, on palpation, a deep mass. This might be felt in the pancreas region but in some cases extended much beyond it, even going well over to the right side. The clinical symptoms were fairly characteristic and the diagnosis could usually be made without urine, and stool examinations, which, to be of value, would be quite complex chemical procedures. Possibly the test for a fat-splitting ferment in the urine might be of use.

Surgical Treatment.

In peripancreatic abscess Dr. Finney said the surgeon could either do nothing or accomplish much by doing little. Opening and drainage were the essential features. If the case was seen early it was better to do this in two stages—the tumor being isolated by gauze in the first and opened in the second after peritoneal adhesions had formed.

February 6, 1905.

Gastric Tetany. Dr. Howard.

Dr. Howard gave the clinical report of a patient who died in the Johns Hopkins Hospital with this condition. The man was 58 years of age and had suffered for years with attacks of indigestion characterized by gastric pain relieved by vomiting. There had never been blood in the vomitus. For three years before admission attacks of vomiting were frequent, large amounts of sour stomach contents being brought up. They were, however, much improved by the regular use of the stomach tube. Previous to this regular lavage there had also been several typical attacks of tetany, but they too disappeared with the use of the stomach tube. The patient, however, began to lose weight and strength and consulted Dr. Osler in November, 1904. A dilated stomach was found, peristalsis was visible and a surgical operation was advised. This was, however, postponed and the patient returned to the hospital in January, 1905, much improved. During his stay in the ward he was one day suddenly seized with epigastric pain (following a dietary indiscretion), and some pain and cramps in the extremities accompanied it. Relief followed the use of a stomach tube; but an attack of tetany supervened. Every muscle of the body went into tetanic contraction, the typical contracture of the hands being present as well as carpopedal spasm. Pain was agonizing, the face became purple and sweating was profuse. Trousseau's symptom was present. For twenty-four hours there was almost complete suppression of urine, and death occurred in forty hours, the patient being in a state of semicoma for the last twelve hours, during which time tetanic attacks were provoked by merely touching the patient's bed. There had been, Dr. Howard said, seven other cases of tetany in the Johns Hopkins Hospital. One was associated with repeated pregnancies, one came on after a severe fright, another was accompanied by a severe diarrhœa, and a fourth by tuberculous meningitis. The remaining three had been gastric cases associated with dilatation, hyperacidity, and hypersecretion. In adults the following forms of tetany were usually recognized: the epidemic, the gastrointestinal, the toxic (chloroform, etc.), and the forms accompanying pregnancy, acute infectious diseases, nephritis, nervous diseases, and thyroid extirpation. The cause of gastric tetany has been much discussed. Kussmall thought that dehydration was the essential feature, others noting the frequent occurrence of attacks of tetany after the use of the stomach tube in patients with the disease, explained the phenomenon as a reflex. Toxines from decomposing stomach contents had also been suggested as an hypothesis to account for the condition and a certain peptotoxin had been isolated by the French. The condition was said to be rare, was usually associated with gastric dilatation, hypersecretion and pyloric stenosis. The disease is very fatal—sixteen deaths occurring in a series of twenty-seven cases collected by Riegel.

The Pathology of Tetany. Dr. MacCallum.

It was to be noticed, Dr. MacCallum said, that the disease occurred in conditions associated with the elaboration of toxines; and there were certain experimental findings which added support to the toxine theory. If, for instance, tetany were artificially produced by extirpation of the parathyroid (*not*, as the books said, of the thyroid) the tetany could then be relieved by removing the animal's blood and replacing it with salt solution. Cure, at least temporary, could also be effected by the use of parathyroid emulsion. The tetany following extirpation of the parathyroids was, in brief, a specific form. The patient reported by Dr. Howard had proven at autopsy to have five pairs of parathyroids instead of the usual four, and these had shown on section numerous mitotic figures (a rare finding in normal parathyroids) as though the parathyroids had become hypertrophied to neutralize large absorption of toxine from the stomach. Dilatation of the stomach was enormous, the capacity being 4¾ liters, and the organ reaching to the right iliac fossa. There was great contraction of the pyloric orifice which measured 5 x 2 mm. Micro-

scopically the tissue at this point did not show the typical picture of a healed gastric ulcer, but Dr. MacCallum was inclined to think that such had been the origin of the pyloric stenosis. The sudden death which occurred so often during the early history of thyroid surgery had been due, he said, to extirpation of the parathyroids. It had ceased to occur when complete thyroid removal ceased to be done, and the reason for this had been that the parathyroids were left in. Sudden death, however, associated with features of intoxication and occurring in goitre patients, was difficult to explain. It had been thought to be due to a leakage of colloid material, but experimental work had shown this to be not the case.

Synaesthesia. Dr. H. L. Smith.

Dr. Smith read a paper on this subject reporting several cases. The word was used, he said, to mean the occurrence of constant and involuntary association of irrelevant subjective symptoms in response to certain stimuli. "Sound-feelings" for example occurred in many normal individuals, the disagreeable shiver when glass is scraped being a familiar instance. "Sight-feelings" were also quite common; and the statement had been made that 12.8% of all persons were normally synæsthetic. The association of letters and musical tones with colors was not infrequently seen and some musicians were said to tune their instruments by color sensations. Number synæsthesia was one of the commoner forms—numbers being conceived of as occupying definite positions in space, usually on a geometrical figure. Statements as to the physiological or pathological nature of this condition varied, but there seemed little doubt that heredity was an important factor in the etiology. The cases reported were all members of the same family, the father, four sons, and two daughters being affected. The synæsthesia took various forms in the different members, the association of colors with letters, of space position with numbers, of ideas (independent of their meaning) with words being prominent forms in the family. Transmission was plainly from the father, and all the members of the family were of a high grade of mental development. In each case the synæsthesia was most intense in youth and faded with the advance of age. Dr. Hurd reported a similar case, the patient being a person of fine intellect and unusual musical talent, but of a nervous temperament. Dr. Thayer reported a case of number synæsthesia in which the calendar was always thought of as being a definite geometrical form (an octogon), each date having its own position thereon. In this patient the alphabet was always thought of as a spiral and there was a definite geometrical scheme for the numbers. No color synæsthesia, however, existed.

Hanging Block Cultivation of Bacteria. Dr. Ford.

Dr. Ford described Hill's method of growing organisms and observing their morphology during their growth. The early discussion as to the nature and classification of bacteria had, he said, obscured their relation to disease and Koch had been led to propound his famous dictum that the biological nature of organisms was immaterial so long as they were constantly found in association with the same disease process. The recent work of Westbrook and of Hill had, however, thrown a good deal of light on the morphology of bacteria. An organism was shown which had been thought to be one of the simple pigmented bacteria but which, in hanging block showed definite mycelial growth.

The Ultraviolet Rays.

Dr. Ford also reported some experiments he had made on the effect of the ultraviolet rays on bacterial growth. A quartz prism, a cadmium spark, and an agar plate of *B. prodigiosus* were used. Within the ultraviolet rays and reaching to the limit of the violet rays (*i. e.*, including all wave lengths from .00034-.0002175) bactericidal action was evident. Beyond these limits there was none.

Thermophilic Bacteria.

During the sterilization of some blood-serum tubes in Dr. Ford's laboratory at 57° C. a growth was found to have occurred on the tubes. The organisms were plated and were found to grow only slightly below 40° C. and rapidly at higher temperatures. They were long, spore-bearing bacilli. Similar organisms have been described by Novy, by the Italians, and by Rabinovitch, who isolated several forms from decomposing manure. The various forms are all much alike, all bear spores and do not grow on ordinary media. They cannot be differentiated except by the fact that some do and others do not liquefy gelatin.

February 20, 1905.

The Cure of Uterine Cancer. Dr. John G. Clark.

Dr. Clark reviewed the recent literature on this subject, drawing conclusions as to operative treatment from the statistical studies which had been published. Radical and complete operation had aroused, Dr. Clark said, bright hopes as to the solution of the problem of the treatment of cervical carcinoma. The ultimate results had, however, been disappointing and led the speaker to take a pessimistic view as to the value of the complete operation. Up to the time of the publication by Dr. Clark in 1896 of a review of the experience of the Johns Hopkins Hospital with uterine cancer vaginal hysterectomy had been the operation done there; and the results of a series of forty-eight cases, though as good as in any hospital, were distressingly bad. It was then suggested that carcinoma of the uterus ought to be treated as carcinoma of the breast had been and an attempt was made to adopt the Halsted procedure for breast and axilla to the uterus and pelvis. Experience with this operation had, however, not given the results hoped for, and Dr. Clark did not think that complete dissection of the pelvis offered much for the future. Absolutely complete removal of all the glands was impossible; the prognosis might still be bad even if all the glands *were* removed; a large proportion of patients are quite inoperable when seen at the clinic; and death has usually been from local recurrence. These facts do not warrant one in expecting results in uterine cancer simi-

lar to those which have been obtained in breast cancer. The composite experience of various operators has also offered nothing to show that the complete operation accomplishes enough to offset its very much greater primary mortality. Reis, among the early writers, thought metastasis an early phenomenon and advocated complete glandular removal. Cullen and others said that metastasis to the glands did not take place early; but Wertheim, studying serial sections, found the glands involved in 31.7% of all cases and claimed that many metastases had been overlooked by others. Schauta, who advocates radical removal of the growth and not a prolonged search for metastases, divides the pelvic glands into six groups—the sacral, the iliac, the aortic, the cœliac, and the deep and superficial inguinal. Groups 1 and 2 are operable; groups 3 and 4 inoperable; while groups 5 and 6 did not usually enter into the question. Schauta reported sixty cases with eleven deaths, the prognosis varying notably with the site of the glandular metastasis. He found also that the extent of the disease was no criterion at all of the extent of the metastasis; and that the *size* of glands was of no clinical value in deciding on whether or not they were involved. No one has yet explained why some early uterine carcinomata metastasize while other late ones do not; nor why certain glands may be skipped by the metastasis; nor why large glands may be free from cancer while small neighboring ones are involved. It is probable that not the glands alone but also the lymph vessels, veins, and surrounding tissues offer routes for the growth. Kundrath has shown that the growth may take place in several ways; first, by mass growth from the cervix, usually circumscribed, but in some cases with finger-like processes; second, association of circumscribed growth with metastases; and third, combinations of 1 and 2. Wertheim, in his 1901 report, said that unless the glands were enlarged they need not be removed. This is now known to be incorrect; but removal of glands, at any rate, is of prognostic and not of curative value. Dr. Clark's own opinion is that more is lost than gained by an attempt at complete glandular removal—a prolonged procedure with high mortality. While he thought the complete operation ought to be given a good trial by careful and competent men he did not expect much from it and personally never did the complete operation—removing all the growth and as much neighboring tissue as possible by means of the cautery (abdominal incision), but making no attempt to get out the glands. Olshausen, who uses vaginal hysterectomy, has reported a series of over six hundred cases, 31% of which were operable, and 18% remained well after five years. As to the future, something might be hoped for from the work being done to develop treatment other than surgical. From the operative standpoint the outlook was not bright. It was absolutely necessary to have the diagnosis made early when the cases could be saved by surgery—and physicians and laity should be educated (as they have been in Germany by the efforts of Winter) to watch all symptoms at the time of the menopause and always to report promptly uterine hemorrhage.

Pathology of Cervical Cancer. Dr. Sampson.

Dr. Sampson reviewed the pathology of this condition as illustrated by the cases seen at the Johns Hopkins Hospital. In the cervix cancer is more frequent than in the fundus, spreads more rapidly, is attended by a higher mortality and a lower percentage of cures. It is the most frequent form of primary cancer, is a disease of midlife and is frequent in those who are bearing children. It thus takes away valuable members of society when they can least afford to be missed. At the present very little is being done by way of surgical cure. Seventy-five per cent of the cases that come to the clinics are inoperable; recurrence occurs in three-fourths of the cases operated upon; and in practically 93% of all cases there has been simply no cure. Early diagnosis and complete removal of the growth—but not of the glands which are, when removed, of prognostic value only—offer the only hope of cure, the cases being curable early and operability increasing the earlier the disease is seen. Sixteen of the cases at the Johns Hopkins Hospital were living five years after the operation and four ten years after. Dr. Cullen said that he used Wertheim's operation, and did not dissect out the glands. Dr. Bloodgood said that the problem in uterine cancer was like the problem in cancer elsewhere; and that an extensive local operation should always be done. In the stomach complete glandular removal was attended by so great a mortality and the chance of recurrence was so great as not to justify the operation. In the breast the problem was simpler. There was practically no mortality from the operation; and, in the cases at the Johns Hopkins Hospital over 45% have remained cured for three years. In cancer of the lip glands were easy to remove, the tumor was usually noticed early, and the mortality of the operation was small.

NOTES ON NEW BOOKS.

The Practical Application of the Röntgen Rays in Therapeutics and Diagnosis. By William Allen Pusey, A. M., M. D., Professor of Dermatology in the University of Illinois; and Eugene W. Caldwell, B. S., Director of the Edward N. Gibbs Memorial X-Ray Laboratory of the University and Bellevue Hospital Medical College, New York. Second edition, thoroughly revised, and enlarged. 690 pages, with 195 illustrations, including four colored plates. (*Philadelphia, New York, London: W. B. Saunders & Co., 1904.*)

The fact that this excellent work has attained the distinction of two large editions in one year is proof of its value.

A practical feature of the work is that nearly all the cases and illustrations are based upon the author's own experience. This edition contains a review of all the literature of X-ray therapeutics to date, and, as the author points out, but little new has been added to our knowledge, yet it is of the utmost value in confirming the earlier claims as to the value of the X-ray from a therapeutic standpoint.

The important feature in the work is the sane judgment of the author upon the therapeutic value of the Röntgen rays in deep-seated neoplasms. His view upon the subject is as follows: "The extravagant hopes of enthusiasts as to the cure of the gravest malignant neoplasms has not been realized, but if this

excessive demand upon it is eliminated, it has more than fulfilled the prospects of usefulness which it at first seemed to offer."

Part I of the work is devoted to apparatus and the technique of radiography. Part II, the larger section, deals with the therapeutic effects. The treatment of the various diseases is taken up in detail and supplemented with reports of a great number of cases. Each chapter has an excellent bibliography attached.

The work is a most excellent one, not only from its usefulness, but also as a book of reference.

Eye, Ear, Nose and Throat Nursing. By A. Edward Davis, M. D., and Beaman Douglas, M. D. With 32 illustrations. (*Philadelphia: F. A. Davis Co., Publishers, 1905.*)

Any nurse who expects to care for cases in the Eye, Ear, Nose and Throat can read with profit the pages of this book. It not only describes in detail the nurse's duties in these cases, but also gives a short account, in simple language, of the diseases themselves, and of the operative procedures undertaken, and thus puts the nurse in a position of coöperating more intelligently with the physician. The book contains a number of valuable suggestive points, which will be found of interest, not only to the nurse, but to the general practitioner as well, into whose hands a large number of these cases fall at first. It is well printed, in the main well arranged, and contains an excellent index.

Appendicitis. By Bayard Holmes, M. D., Professor of Surgery in the University of Illinois, Attending Surgeon Chicago Baptist Hospitals. (*New York: D. Appleton & Co., 1904.*)

While the greater part of this book is devoted to the subject of appendicitis, certain other diseases of the abdomen are discussed, namely, peritonitis, intussusception, perforating typhoid ulcer, and carcinoma of the intestinal tract.

Appendicitis is discussed thoroughly and in a most interesting manner. There is a short account of the history of the disease and then the anatomy of the appendix and the pathology, symptomatology, diagnosis, complications and treatment of appendicitis are considered.

The author discusses briefly the origin of pain in appendicitis and calls attention to the fact, now generally known, that the visceral peritoneum is practically insensitive to pain, whereas the parietal peritoneum is exquisitely sensitive. He says, "the origin of pain in appendicitis is hard to explain and no absolute demonstration of it has yet been given."

He gives a good, but perhaps somewhat exaggerated account of those cases of chronic appendicitis giving rise to indefinite and varied symptoms, the cases sometimes known as "grumbling appendices."

In the chapter on the complications of appendicitis the author mentions the cases with abscess involving the iliacus muscle, causing flexion of leg, etc., cases with subphrenic abscess and those with gangrene of ileum or cæcum. Among the complications and sequelæ, he does not mention post-operative intestinal obstruction, which is not a rare occurrence in most hospitals.

He condemns those who recommend the so-called expectant method of treatment in certain acute cases of more than 24 hours duration.

The author allows many of his cases to get up on the second day and to leave the hospital in four to five days. It seems to us that this is unnecessary haste.

An Introduction to Vertebrate Embryology, Based on the Study of the Frog and the Chick. By Albert Moore Reese, Ph. D. (Johns Hopkins), Associate Professor of Histology, Syracuse University. (*New York: G. P. Putnam's Sons, 1904.*)

This little book is designed to give in a brief and convenient form an outline of the development of the common frog and the chick. As the author has stated, it is largely a compilation from larger and more expensive books such as Marshall's or Minot's Embryology. It gives an outline of the main stages in the embryological development and will be of service to those who wish a general survey of the subject without going deeply into it. The medical student will find that histology and pathology are only to be grasped clearly from the point of view of development and hence he will do well to gain as clear an idea of embryology as possible. The book is well illustrated, there being 84 figures selected wisely from various sources.

Atlas and Epitome of General Pathologic Histology. By Dr. H. Dürck, of Munich. Edited, with additions, by Ludvig Hektoen, M. D., Professor of Pathology, Rush Medical College, in affiliation with the University of Chicago. With 176 colored figures on 80 lithographic plates, 36 text-cuts, many in colors, and 371 pages of text. (*Philadelphia, New York, London: W. B. Saunders & Co., 1904.*)

This volume, which treats of various general processes in pathology such as degenerations, inflammation, repairs, etc., and of tumors, is part of the work on Pathology by H. Dürck, of which the portion devoted to special pathological anatomy has already been reviewed. It is the translation from the German edition, edited with many notes by Prof. Hektoen. The text reveals Prof. Dürck's broad knowledge of pathology and of literature on the subject toward which he maintains a critical attitude. It is strikingly clear, logical and sane throughout, and Prof. Hektoen has secured for it a pleasing English style.

The illustrations, though, are incomparable, both on the judicious selection of the preparations for which they were drawn, and from the wonderful perfection of their execution. The drawings of the tumors are not all so good as those in the first part of the book, but even so they are approached only by those of Borst's book on tumors. Finer illustrations have rarely been seen in any medical publication.

These plates together with the excellent text make the book extremely valuable to students, and should give it a place among the best works on pathology that have been printed in English.

International Clinics. A quarterly of illustrated clinical lectures. Edited by A. O. J. Kelly, M. D. Fourteenth series, Vol. III. (*Philadelphia: J. B. Lippincott Co., 1904.*)

The first part of this volume is devoted to discussion of certain phases of syphilis and its treatment, the most notable being a thorough review of the hypodermatic methods of treatment by Fournier.

Of more general interest is Lawrason Brown's contribution on the digestive disturbances in tuberculosis. This is a close and detailed study of a subject of much importance and full of practical information, preventive, dietary, and therapeutic, which Dr. Brown has drawn from his experience at Saranac and from the literature. T. R. B.

A Text-book of Pathology for Practitioners and Students. By Joseph McFarland, M. D., Professor of Pathology and Bacteriology in the Medico-Chirurgical College, Philadelphia. With 350 illustrations. (*Philadelphia, New York, London: W. B. Saunders & Co., 1904.*)

A volume of about 800 pages with numerous illustrations, of which part are original, is added to our list of text-books of Pathology. Ten chapters are devoted to general pathology and ten to the special pathology of various organs. On the whole the book is good as far as it goes. Mention is made of nearly everything that one might expect to find described in a text-book of

pathology, and with a few exceptions the statements are correct. The book is characterized, however, by an extraordinary conciseness, such that the least advanced student must remain dissatisfied with what he finds on any particular subject. While the brief statements correspond well with the current opinion, this seems to be rather the result of success in consulting the best author upon the subject than of a wide consideration of the literature. More recent discoveries and the newer publications are very summarily dismissed. The original illustrations are not very good and there is practically nothing new in the book, either in text or method of arrangement. It is very doubtful whether such a summary, much of which consists essentially of definitions, is what is needed by students of the present day who have the intelligence and the will to read such living descriptions as are found in Orth's text-book and are not merely anxious to prepare for examinations.

Diseases of the Ear, for Practitioners and Students of Medicine. By James Kerr Love, M. D., Aural Surgeon, Glasgow Royal Infirmary; Lecturer in Aural Surgery, St. Mungo's College, Glasgow; etc., etc. With 54 Stereographic Photographs, 2 colored plates and many illustrations. (*Published by John Wright & Co., Bristol; and Simpkin, Marshall, Hamilton, Kent & Co., Ltd., London.*)

A very excellent work and one that is sure to meet the approval of the otologists. The concise, practical manner in which the really important subjects of otology are treated will appeal not alone to the student but to the busy physician. It is a book that one can really read with sustained interest for there is not a word too much said of any subject. It is, altogether, a strong presentation of practical otology.

It is the first time I have seen stereographic photography used in a text-book, and I am not sure it will prove a complete success. The pictures are excellent and I have long expected that some one would use just this method of illustrating the temporal bone, which is so difficult to show by ordinary photography or by drawing, but it is not easy to examine them as bound in the book. I hope the plan will meet with general favor. H. O. R.

Modern Ophthalmology, A Practical Treatise on the Anatomy, Physiology and Diseases of the Eye. By James Moores Ball, M. D., Professor of Ophthalmology in the St. Louis College of Physicians and Surgeons. With 417 illustrations in the text and 21 colored plates. (*Published by the F. A. Davis Co., Philadelphia.*)

The title of this book is certainly well chosen for the author has evidently tried to give us a book befitting the period. I know of no other single volume text-book of Ophthalmology that approaches this one in completeness of subjects considered; every conceivable affection of the eyes has been mentioned and, in most instances, the very latest knowledge concerning each topic is given.

The publishers, too, deserve commendation; the paper, the print and the illustrations are of the best. H. O. R.

First Report of the Anti-Malarial Operations at Mian-Mir, 1901-1903. By Capt. S. P. James, M. B. (Lond.), I. M. S. (on special duty). (*Office of the Supt. of Government Printing, Calcutta, 1903.*)

This report, which is issued under the authority of the Government of India, contains a detailed account of the investigations initiated by the Royal Society's Malaria Commission with the intention of demonstrating experimentally that malarial fevers can be prevented by practical measures based on the discovery that a particular species of mosquito is the definitive host of the malarial parasite. It is impossible to do justice to this interesting piece of work in the space available here, but the most important conclusions are these:

There appears to be no doubt that *anopheles culicifacies* is the chief, if not the only carrier of malarial organisms in Mian-Mir, which is one of the most unhealthy cantonments in India. The source of infection in the Royal Artillery Lines, where the investigation was carried on, was, beyond doubt, the children in the various Bazaars and followers lines. The results of the research show conclusively that the destruction of this species of mosquito, if carried out successfully, will effectually banish malaria, but such destruction is materially hindered by its difficulty and expense. In this connection, however, great importance is attached to the second set of experiments, namely, the attempt to lessen the effects arising from the obvious sources of infection in cantonments. It has been shown that this can be done by treating large numbers of native children regularly with quinine, and as this is a measure requiring no special knowledge and involving no great expense, it is applicable to every place where large numbers of native children are gathered in the vicinity of European troops.

The report is well worth reading by anyone interested in the subject, for it contains a great deal of interesting matter which cannot be condensed.

Traité d'Hygiene Procédés rapides de Recherche des Falsifications et Altérations. Par Dr. P. Smolensky, de St. Petersbourg; translated from the Russian by S. Brömo and A. Zaquelmann. Two volumes. (*G. Steinhal, Paris, 1904.*)

The early part of this work is devoted to the description of methods for analyzing the food-stuffs in ordinary use and of a character sufficiently simple and inexpensive to permit their being used in boarding-houses, asylums, hospitals, and even in private houses. The latter part deals with the hygienic questions associated with light, heat, clothing, the choice of dwelling houses, and other kindred subjects. The work contains much useful information and is well adapted for its purpose.

A Hand-book of Surgery. For Students and Practitioners. By Frederic R. Griffith, M. D., Surgeon to Bellevue Dispensary, etc. (*Philadelphia, New York, London: W. B. Saunders & Co., 1904.*)

This work can hardly be considered more than a compend. It shares with so many works of this kind the advantage of being pocket-size, and has for its recommendation the fact that it is neatly bound in flexible cover; the paper used is of good quality and the type is large and clear.

The whole field of Surgery, including the specialties, is briefly outlined and there are brief chapters on Medico-Legal Surgery, Surgical Pathology and Technique.

The 417 illustrations, diagrammatic for the most part, supplement the text fairly well.

To the Practitioner its value will necessarily be very limited; to the Student preparing for quizzes and examinations it can be recommended as one of many.

The Channels of Infection in Tuberculosis. Being the Weber-Parkes Prize Essay, 1903. By Hugh Walsham, M. A., M. D. Cantab., F. R. C. P. (*London: John Bale, Sons & Danielsson, Ltd., 1904.*)

The Weber-Parkes Prize is given triennially by the College of Physicians in London for the best essay on some subject connected with tuberculosis, especially with reference to pulmonary tuberculosis in man. This prize was awarded to Dr. Walsham, in 1903, and this volume contains the essay.

The greater part of the work is taken up with discussion of the channels of infection. The work impresses one as rather a discussion of some of the questions coming under the head of infection, than a broad, comprehensive survey of the subject. Dr. Walsham is led into the discussion of side issues, which, however, are most important and of great interest. Thus he discusses the relationship of scrofula and tubercle. He has studied a number of cases at autopsy and comes to the conclusion that the so-called scrofulous gland is really a tuberculous one.

The channels of infection are considered under five headings:

1. Heredity.
2. Lymphatic vessels.
3. The blood-vessels.
4. Epithelial channels.
5. Inoculation.

Perhaps the most interesting section is the discussion of the question as to the frequency with which tubercle bacilli are absorbed by the tonsil or adenoid tissue. Out of thirty-four consecutive post-mortem examinations the tonsils were found to be more or less tuberculous in twenty. In some of these cases the tonsillar infection was perhaps secondary to the lung, but in others the primary source of infection seemed to be undoubtedly in the pharynx. The examination of tonsils and adenoid vegetations removed from the living patient was entirely negative. From his studies Dr. Walsham has come to the conclusion that the tonsils are very frequently affected. There is considerable space given to the question of renal infection.

The second part of the book takes up the conditions which render the tissues vulnerable; the relationship of alcohol, diabetes, cardiac disease, cancer, etc., to tuberculosis are dealt with.

Mention should be made of the illustrations, which are numerous and satisfactory.

Diseases of the Liver, Gall-bladder and Bile-ducts. By H. D. Rolleston, M. A., M. D. (Cantab.), F. R. C. P., Physician to St. George's Hospital, London. (*Philadelphia, New York, London: W. B. Saunders & Co., 1905.*)

To write a good book on any subject is difficult, but to write a good book on diseases of the liver would seem especially so. Those who have known Dr. Rolleston's work in the past have looked forward with much interest to the publication of this book, a work more ambitious than any he has yet done. Dr. Rolleston has had the advantage of a thorough training in pathology, the usefulness of which in clinical medicine cannot be over-estimated. The present volume is a model of what such a work should be. It discusses subjects in a broad way, and at the same time contains a perfect mass of details, well arranged and easy of reference. There does not seem any doubt that this is the best work we have on the diseases of the liver. Murchison's work is, of course, well-known but since its publication there have been many advances along various lines.

Dr. Rolleston, very wisely we think, omitted any description of the anatomy and physiology of the liver. The book opens with a short section on some anatomical abnormalities, some common post-mortem appearances and acquired deformities. Following this is a section on displaced and movable liver. After this is a chapter on functional disease. When we consider the important place which this takes in the popular mind (and we fancy to a greater extent in this country, especially the South, than in England) we realize its importance. Dr. Rolleston believes that many symptoms often attributed to the liver are really due to gastric and intestinal conditions. He emphasizes the importance of the treatment of these other conditions. The various disturbances of the portal circulation are discussed and the various morbid conditions of the lymphatic vessels. Changes in the liver secondary to cardiac conditions are described and there is an interesting section on pericarditic pseudo-cirrhosis. Acute congestion and acute hepatitis are also discussed.

The section on abscess of the liver is an interesting one. Dr. Rolleston points out the many difficulties of accounting satisfactorily for the etiological factors of some cases. There can be no question that amœbic abscess of the liver occurs without any dysentery, but it is only after the most careful examination of the bowel that the absence of intestinal lesions should be considered as proved. In a recent case one very small, almost healed ulcer, in the colon, was recognized only after most careful search. This should be kept in mind, as probably cases have been reported as having a normal colon in which a very slight ulceration had been overlooked.

The section to which one turns with the greatest interest is that dealing with cirrhosis. Various classifications are quoted but the author concludes that for practical work it is best to make a division into two probable types, (a) ordinary or common cirrhosis (portal), (b) biliary cirrhosis. A good comparison is made with some forms of kidney disease, portal cirrhosis being compared to a granular kidney and hypertrophic biliary cirrhosis to chronic parenchymatous nephritis. The terminal production of multilobular cirrhosis in a long-standing hypertrophic biliary cirrhosis corresponds to the contracting kidney following the large white kidney. There are so many interesting points which might be discussed in this connection that it is difficult to choose. For example, the cause of splenic enlargement in cirrhosis. Dr. Rolleston inclines to the toxæmic theory. There is a great amount of detailed information regarding the various conditions, as for example hæmatemesis, the discussion of which is exceedingly good. A point of great interest is as to the relationship of ascites to chronic peritonitis. Hale White considers that cases of cirrhosis with ascites but without chronic peritonitis never survive to be tapped more than once. It would be well if this point could be definitely settled. The subject of hæmochromatosis receives adequate notice. Biliary cirrhosis is taken up at some length and a very clear description given. It is impossible to do justice in a review to this section on cirrhosis. It seems one of the best descriptions of the subject which we have in English.

Tuberculous and syphilitic diseases of the liver follow. We should agree with Dr. Rolleston in thinking that hepatic syphilis is very often overlooked, and he does well in emphasizing the importance of bearing in mind the possibility of syphilis in obscure enlargements of the liver. There is a section on hydatid cyst and on fatty and lardaceous diseases of the liver.

Malignant disease of the liver is taken up under the headings of primary and secondary and many statistics are quoted. Very many doubtful points associated with jaundice are well discussed. The cases are divided into two classes, (a) the extra-hepatic or obstructive, (b) the toxæmic or intra-hepatic. The many causes which may give rise to jaundice are taken up at considerable length. If we ventured to make one suggestion it would be that Dr. Rolleston might have laid greater emphasis on the dangers of hæmorrhage from operations done on patients with jaundice. Preliminary treatment with calcium salts may greatly diminish the risk of bleeding at operation.

The second part of the book deals with diseases of the gall-bladder and bile-ducts. Acute cholecystitis and tumors of the gall-bladder are taken up first. The section on cholelithiasis is an excellent one. The diagnosis is fully discussed. The author takes perhaps the moderate view as to surgical treatment. During an attack of colic an operation is justified only if there be a special complication which might prove fatal, such as a rupture of the gall-bladder, etc.

In reference to operation after repeated attacks Dr. Rolleston takes a rather non-committal attitude, which is perhaps the safer

course, but the general tendency in the profession would seem to be to advise operation more frequently. The section on the general treatment of patients with gall-stones is a very excellent one.

The sections on morbid anatomy and histology are clear and satisfactory. In the discussion of the clinical material there is an excellent arrangement. The heads under which the various features are described are well separated and the reader has a clear idea of the whole subject as presented. Although many cases are quoted, they have been judiciously extracted and only the essential features are given. The material from St. George's Hospital has been extensively used. There are many references and it is pleasing to see how carefully the American literature has been extracted. The illustrations are good and there are a number of colored plates. Altogether we regard this as a most satisfactory work, and extend our congratulations to Dr. Rolleston on its success.

An Introduction to Pharmacognosy. By SMITH ELY JELLIFFE, M. D., Ph. D., Professor of Pharmacognosy in Columbia University. (*Philadelphia, New York, London: W. B. Saunders & Co., 1904.*)

This book is published with the intention of giving a work in compressed form dealing with the general anatomical characters of drugs. Dr. Jelliffe has described both their macroscopical appearances and microscopical characteristics. As the author points out, pharmacognosy may be approached from several sides, for example from the botanical point of view, the histological aspect or the special study of the constituents of the plant.

The book opens with a description of animal drugs, under which the leech and cantharis are described. Naturally the greater part of the work deals with vegetable drugs. The method pursued is to describe first the gross characters of the structure and then the histology, with a note regarding the chemistry. The descriptions are clear and the illustrations are satisfactory and helpful. The work seems to be admirably adapted for the purpose kept in mind and should be very useful to students of the subject.

Adolescence: Its Psychology, and its Relation to Physiology, Anthropology, Sociology, Sex, Crime, Religion, and Education. By G. STANLEY HALL, Ph. D., LL. D., President of Clark University and Professor of Psychology and Pedagogy. Two Volumes. (*New York: D. Appleton & Co., 1904.*)

Two methods suggest themselves for the accomplishment of the task the author of these notable volumes sets for himself. One consists of a simple statement of the facts of adolescence in their various relations; and the other, a most difficult, Herculean feat, the organization of these facts and their relation into a systematic philosophical study. The reader need hardly be told that to the latter Stanley Hall has addressed his energies. Many will recall the incident, made the subject of a newspaper story a few years ago, of the ambitious American student, who was given, as an initial task by his German professor, the study of a frog's muscle. Few know that Stanley Hall was the student. In his words, "The mild dissipation of a somewhat too prolonged general culture and a little taste for easy, breezy philosophical speculation caused at first a strong sense of repugnance from so small and mean a theme. When it was well under way, however, and with the daily and personal guidance of this master in devising methods of experiment, planning new instruments for record and stimulus, suggesting fertile possibilities, showing the details of all the technique, suggesting and placing in my hands new reading, etc., I found that I must know in a more accurate way than before certain definite points in electricity, which was the agent of stimulation; in mechanics, for the apparatus was complex, and there were possibilities of improvement and invention that might open up a new field of myological investigation; in the anatomy and physiology of other tissues for comparison; in chemistry, in order to judge something of the effects of the artificial blood for constancy; and in mathematics in order to compute and analyze the contraction curve into its components and to construct and interpret the records and tables. . . . As the work went on, I felt that the mysteries not only of motor education and morality, but of energy and the universe, centered in this theme, from the persistent study of which, although in the end I made but an infinitesimal contribution to the vast body of certain scientific knowledge in the world, I learned several great lessons, viz.: that any object, however unattractive, may be a key to the greatest themes; that narrow specilization is now hardly possible."

This reveals the author's method. The reason lies not only in the large number of adolescents, "one-third of the inhabitants of America and all so-called heathen people," but in the vast importance of this period of life, in which individual character is developed, formed and completed, and in the light of which all subsequent personal history is but a repetition or a demonstration of the destiny nurtured in adolescence, the "most fascinating of all themes, more worthy perhaps, than anything else in the world of reverence, most inviting study, and in most crying need of a service we do not yet understand how to render aright. . . . Here the young appeal to and listen to each other as they do not to adults, and in a way the latter have failed to appreciate. Again, no biography, and especially no autobiography, should henceforth be complete if it does not describe this period of transformation, so all-determining for future life, to which it alone can often give the key. To rightly draw the lessons of this age not only saves us from waste ineffable of this rich but crude area of experience, but makes maturity saner and more complete."

The work consists of two royal octavo volumes of, respectively, six hundred and seven hundred and fifty pages. In a general way the division into volumes represents a distinction between the physical and the mental or spiritual aspects of the subject. The eight chapters of Volume One are entitled Growth in Height and Weight; Growth of Parts and Organs during Adolescence; Growth of Motor Power and Function; Diseases of Body and Mind; Juvenile Faults, Immoralities, and Crimes; Sexual Development: Its Dangers and Hygiene in Boys; Periodicity; Adolescence in Literature, Biography and History.

It is not possible, even with generous allotment of space, to outline fairly in a review the scope of these topics. True to his own adolescent discipline in the investigation of the ranal gastrocnemius, the author describes the growth and function of the human body, not only by compilation of all available statistics, but by careful analogies with the life histories of all human and feral races and types. Thus the infantile movements of swimming are correlated with the stage of embryonic existence in which ichthyic evolution is represented; and the later phases of extra-uterine growth are shown to be represented, first in feral, later in savage ancestry.

From the category of diseases the author passes to juvenile faults, immoralities and crimes. Monstrosities, idiots, vagrants, itinerants, vagabonds, gadabouts, hoboes and tramps, their tendencies, sentiments and acts, make a most absorbing chapter. We may say, as Longfellow said of Dickens, "He is prodigal and ample, but what a crowd of villains he contrives to introduce us to." The reader who takes up the volume casually for pleasure and profit finds in the later chapters compensation for the tedious mustering of dry facts with which it opens. As in fiction, the initial chapters delineate the characters, who later display their passions, ambitions, purposes and ends. Here these culminate in

the eloquent chapter entitled Periodicity, the apotheosis of the feminine adolescent, revealing the deep pedagogical insight and affectionate instincts of the author's ideals. There exists, perhaps, no better analysis of the characteristics of sex, and his pleas, not only here but elsewhere, for the preservation of the complementary attributes of men and women, and his protests against their destruction, by whatever means;—the virilization of the one, and the feminization of the other, must stand as the strongest thesis of the many he attempts. In education, religion, mental training of whatsoever sort, this deplorable tendency is condemned. He strikes a forcible blow in a practical way at one source of feminine depreciation: "There are now, happily, signs of a reaction against the recent excessively surgical tendency, which has been too dominant, toward a larger view of the whole life of woman. Specialists are beginning to realize that they must broaden their view from the pathology of her organs, till lately so often doomed, if she once consulted them, to the entire problem of regimen, and know at least as much about woman as about her pelvic diseases. Indeed, not a few experts are beginning to recognize that this larger field is relatively unknown to them, and that they must begin the study of the new or higher gynecology with something like a Socratic confession of ignorance. As long as they hold any exclusive theory which consigns to either ovaries, tubes, or central nervous system, the exclusive dominance, or assume that either the psyche or soma is always primal or causal, little progress can be made. Each of the modern views is partially correct and must always be considered as a possible aspect of each case."

Volume Two consists of Chapters Nine to Eighteen inclusive, entitled: Changes in the Senses and the Voice; Evolution and the Feelings and Instincts Characteristic of Normal Adolescence; Adolescent Love; Adolescent Feelings toward Nature and a New Education in Science; Savage Public Initiations, Classical Ideals and Customs, and Church Confirmation; The Adolescent Psychology of Conversion; Social Instincts and Institutions; Intellectual Development and Education; Adolescent Girls and their Education; Ethnic Psychology and Pedagogy, or Adolescent Races and their Treatment.

The second volume to greater extent than the first is liberally illustrated by what in medical language would be termed a casuistry. The author's text is thus elaborated by sketches of Social Instincts and Institutions, including the student's organization of all countries, and associations of youth. The customs and histories of the races in "relation of greater or less subjection to a few civilized nations," the "Adolescent Races," are quite fully extracted from authoritative sources. The author's purpose in this coaptation of civilized youth and barbaric manhood is two-fold; first, the ethnic establishment of the adolescent in nature; and, second, as a plea for the uplifting of inferior humanity, for "every vigorous race, however rude and undeveloped, is, like childhood, worthy of the maximum of reverence and care and study, and may become the chosen organ of a new dispensation of culture and civilization. Some of them now obscure may be the heirs of all we possess, and wield the ever-increasing resources of the world for good or evil, somewhat perhaps according as we now influence their early plastic stages, for they are the world's children and adolescents."

In this closing sentence the author again, and finally, reveals his great sympathy as a teacher and leader of youth. Upon the apprehension of this sentiment by his readers will rest the success or failure of his book. From the enormous mass of material at his hand this professional instinct stands boldly forth, and beside it, the ventures into other fields sink into comparative insignificance. Thus arises question of his denial of the modern conception of "Narrow specialization." He has "tried to bring the subject-matter of each chapter within the reach of any intelligent reader." There are few "intelligent readers" qualified to exercise discriminating judgment upon such variant philosophies as those of religion, art, education, medicine, psychology, sociology and evolution. And a reasonable doubt may be expressed of the author's fitness to treat from the pedagogue's chair of the most disputed questions of conversion or of mental medicine. Surely the discussion of "dementia præcox" has not yet reached the stage when it may be easily handled by a layman. And in no medical treatise would such rhetorical blunders as "plexi" and the "Island of Kiel" escape the proof-readers of one of the most famous publishing houses of the world. The need of "narrow specialization" is still apparent. The phraseology of the author may be also open to question. It is difficult to comprehend very many of his statements without laborious analysis of his sentences. Students of medicine who are acquainted with the verbal simplicity of the German masters, who always reduce the most difficult problems to the simplest expression, so that all science becomes at once practical, will be surprised that stilted language should parade, even indirectly, under the ægis of Professor Ludwig, the hero of the frog's muscle. And the genial and plain-spoken Autocrat would writhe under the appellation given his "ophidian medicated novel, Elsie Venner."

Books inevitably assume one of two forms. They either contain the ideas of the author in the language developed in his processes of thought, which may prove ambiguous; or they set forth in plain, easily comprehended phrases, the crystallized results of thought, which carry a distinct meaning or conviction to the simplest reader. Stanley Hall's book may be placed in the first category, and must lose largely in effectiveness. It appears rather meristic and somewhat banausic in its treatment of the ephebic problems. In his psychonomic recapitulatory impulses the author reveals a trace of solipsism, which is thus found characteristic not of adolescence alone.

In spite of these defects the work is epochal. It centers attention upon the period of life in which character is developed. It reveals a marvellous amount of research and a most acute and analytical observation. The hope may be expressed that in abridged form, in simple diction, the author's knowledge of the training of youth, freed of compilations from philosophical fields in which he is but an observer, may be made available to all thinkers, the world over, who value the force in civilization of strong men and pure women.

J. M. Mosher.

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CONTENTS.

PAGE

Hyperplasia of the Chromophile Cells of the Hypophysis as the Cause of Acromegaly, with Report of a Case. By Dean D. Lewis, M. D., ... 157

The History of the Circulation of the Blood—Contributions of the Italian Anatomists and Physiologists—their Bearing upon the Discovery by Harvey. By John C. Hemmeter, Phil. D., M. D., etc., ... 165

Comparative Surgery; with Illustrative Cases, by C. M. Faris, H. C. Thacher, J. F. Ortschild, and F. C. Beall; and an Introduction by Harvey Cushing, ... 179

PAGE

Correspondence, ... 199

Proceedings of Societies:

The Johns Hopkins Hospital Medical Society, ... 200

Résumé of History of Blood Platelets [Dr. Osler];—The Scope and Problems of Surgical Physiology [Dr. Crile];—Partial Occlusion of the Aorta [Dr. Halsted];—The Blood Pressure in Different Parts of the Arterial Tree [Dr. Dawson];—Heart Block in Mammals [Dr. Erlanger].

Notes on New Books, ... 202

Books Received, ... 204

HYPERPLASIA OF THE CHROMOPHILE CELLS OF THE HYPOPHYSIS AS THE CAUSE OF ACROMEGALY, WITH REPORT OF A CASE.

By Dean D. Lewis, M. D.

[*From the Pathological Laboratory of Cook County Hospital and the Anatomical Laboratory of the University of Chicago.*]

Observations of the clinical and anatomic changes in acromegaly have been reported with increasing frequency during recent years. In all but two of the forty-nine cases collected by Furnivall[1] in 1898, the hypophysis was larger than normal. Four additional cases in which the necropsy revealed no enlargement of the gland have been reported by other investigators: Virchow's[2] case Mennig, the brothers Hagner observed by Friedreich[3] and Erb,[4] and the case reported by Sarbo.[5] The brothers Hagner should be classified as doubtful cases, as Marie was inclined to believe that the changes presented by them were not typical of the disease; in all probability the case reported by Sarbo is to be regarded as an hypertrophic osteoarthropathy of pulmonary origin.

A great variety of pathologic conditions have been described in the hypophysis in those cases of acromegaly in which it has been enlarged and obviously diseased, e. g., simple hypertrophy, twice; adenoma, seven times; sarcoma (variety not specified), five times; large-cell sarcoma, six times; cystic tumors, twice; hypertrophy and colloid degeneration; marked colloid degeneration and hemorrhage; sarcoma or glioma, spindle-cell sarcoma; cylindroma; round-cell sarcoma, glioma, adenoma with enlargement, one each.[6]

The variety of lesions of the hypophysis described in cases of acromegaly is almost equalled by the divers pathologic conditions in the gland, with no symptoms of the disease, as

[1] Furnivall, P.: Pathological Report on a case of Acromegaly, with the Analysis of the Results of 49 Post-Mortem Examinations on Cases of Acromegaly. Tr. Path. Soc., Lond., 1898, XLIX, 204-217.

[2] Virchow, R.: Ein Fall und ein Skelet von Akromegalie. Berl. klin. Wchnschr., 1889, XXV, 81-85.

[3] Friedreich, N.: Hyperostose des gesammten Skelets. Virchow's Arch., 1868, XLIII, 83-87.

[4] Erb, W.: Über Akromegalie (Krankhaften Riesenwuchs). Deutsches Arch. f. klin. Med., 1888, LXII, 296.

[5] Sarbo. (Abstract by Joseph Collins.) J. Nerv. and Ment. Dis., 1893, VIII, 57.

[6] Mitchell, L. J., and Le Count, E. R.: Report of a Necropsy in a Case of Acromegaly with a Critical Review of the Recorded Pathologic Anatomy. N. Y. M. J., 1899, LXIX, 517, 556, 595.

Erdheim's [7] and Breitner's [8] cases of adenoma; Ponfick's [9] of tumor (variety not specified); Packard's [10] of hypertrophy; Cagnetto's [11] of telangiectatic sarcoma; Benda's [12] cases of sarcoma of the periosteum or dura of the sella turcica compressing the hypophysis and teratoma of the infundibulum; Woollcombe's [13] case of psammoma; Beadles' [14] and Hektoen's [15] cases of gumma; Beadles' of tuberculosis and Hinsdale's [16] of sarcoma and finally Bassoe's [17] case in which the hypophysis weighed 5.9 g. and another in which a small calcareous nodule was found in the gland, both without symptoms of acromegaly.

The gland may be completely destroyed without any symptoms of acromegaly intervening. One of the most notable examples of this is the case observed by Weir Mitchell [18] in which destruction of the gland was caused by an aneurysm, arising from an anomalous branch of the circle of Willis. The patient experienced no symptoms, except those directly referable to the aneurysm.

The results following experimental removal of the gland have been indefinite and contradictory. Horsley [19] has extirpated the gland and reports no physical or mental changes. Gley,[20] after experimental removal of the thyroid gland and spleen, extirpated the hypophysis, and found that the symptoms following this extensive operation did not differ from those following removal of the thyroid alone. Vassale and Sacchi [21] noted that after extirpation of the gland animals suffered from dyspnœa, anorexia, depression of temperature, emaciation, tonic and clonic spasms and fibrillary twitchings. One animal survived the operation one year. No conclusions concerning the effects of complete removal of the gland can be drawn from reports which are so wanting in uniformity.

The apparent lack of similarity in the pituitary changes described in cases of acromegaly, the absence of evidences of acromegaly in instances of marked disease of the hypophysis from syphilitic or other chronic inflammations of the granulomatous type, the contradictory results following complete destruction or experimental removal of the gland, and finally the occasional observation of cases of acromegaly in which the gland is of normal size and apparently not diseased, have inclined many investigators to discredit Marie's theory that disease of the hypophysis is to be regarded as the causative factor in acromegaly. It has been suggested that the enlargement of the gland is secondary to enlargement of the sella turcica.

Other theories have been advanced to explain the symptom-complex, chief among which are the following:

1. Nervous theory (Magendi and von Recklinghausen). The disease is supposed to be dependent upon changes in the nervous system.

2. Theory of growth anomaly (atavistic, Freund and Campbell). Acromegaly is not to be regarded as a disease proper, but as an anomaly of growth, the whole appearance suggests a reversion to the anthropoid ape type.

3. Thymus theory (Klebs). This theory suggests that an increase in the vascular canals of a large and persistent thymus is the etiological factor.

4. Genital theory. Acromegaly is accompanied in the majority of females by an early menopause, and in males by impotence; hence the assumption that by the loss of function of the organs of generation an excess of blood is diverted to the extremities, resulting in their hypertrophy.

5. Thyroid theory. Diseased conditions of the thyroid gland, which are occasionally found in acromegaly, are regarded as the causative factor.

All of the foregoing theories have met with serious objections and it has been found impossible to bring the contradictory observations into accord by means of any one of them. The refinements in histologic technic and consequent increase in our knowledge of the minute structure of the hypophysis have succeeded however in lending support to the theory that acromegaly is caused by an excessive function of the cellular elements of the anterior lobe of the hypophysis.

Benda [22] in a recent article, in which he reports the histological changes in the hypophyses of four cases of acromegaly, comes to the conclusion that the hypertrophy and hyperplasia

[7] Erdheim, J.: Zur normalen und pathologischen Histologie der Glandula thyreoidea, parathyreoidea und Hypophysis. Beiträge z. path. Anat. u. allg. Pathol., 1903, XXXIII, 158-232.

[8] Breitner, E.: Zur Casuistik der Hypophysistumoren. Virch. Arch., 1883, XCIII, 367.

[9] Ponfick, E.: Uber Myxœdema u. Akromegalie, Münch. med. Wchnschr., 1899, XLVI, 1358.

[10] Packard, F. A.: A case of Acromegaly and illustrations of two allied conditions. Amer. J. M. Sc., 1892, CIII, 657-669.

[11] Cagnetto, G.: Über die Anatomische Beziehung zwischen Akromegalie und Hypophysisgeschwulst. 2 Riun. Soc. Ital. di Patol., Abstracted in Ziegler's Centralbl., 1904, XV, Nos. 16 and 17, 688.

[12] Benda, C.: Über den normalen Bau und einige pathologische Veränderungen der menschlichen Hypophysis Cerebri. Arch. f. Anat. u. Physiol., Physiol. Abth., 1900, 373-380.

[13] Woollcombe, W. L.: A case of Virchow's Psammoma of the Pituitary Body with remarks as to the function of that structure. Brit. M. J., Lond., 1894, I, 1351-1353.

[14] Beadles, C.: Gummatous Enlargement of the Pituitary Body. Brit. M. J., Lond., 1896, II, 1775.

[15] Hektoen, L.: Gumma of the Hypophysis. Trans. Chicago Path. Soc., 1896, II, 129.

[16] Hinsdale, G.: Akromegaly. Medicine, 1898, IV, 441-637.

[17] Bassoe, P.: Gigantism and Leontiasis Ossea, with Report of the case of the Giant Wilkins. Jour. of Nerv. and Ment. Diseases, 1903, XXX, 513-595.

[18] Mitchell S. Weir: Aneurysm of an Anomalous Artery causing antero-posterior division of the chiasma of the optic nerves and producing bi-temporal Hemianopsia. J. Nerv. Ment. Dis., 1889, XVI, 44-62.

[19] Horsley, V.: Functional nervous disorders due to loss of thyroid gland and pituitary body. Lancet, Lond., 1886, I, 3-6.

[20] Gley, E.: Recherches sur la fonction de la glande thyroide Arch. de Physiol., 1892, t. XL, 311-326.

[21] Vassale and Sacchi: Sulla distruzione della ghiandola pituitaria. Riv. Sperim. di Freniat., 1892.

[22] Fränkel, Stadelmann A., Benda, C.: Klinische und anatomische Beiträge zur Lehre von der Akromegalie. Deutsche med. Wchnschr., 1901, 513, 536, 564.

of the chromophile cells, probably indicating an excessive activity of the gland, are the important factors in the production of the disease; he also considers that mistakes in anatomic diagnosis accounts for the lack of uniformity in the descriptions of the lesions of the hypophysis associated with the disease. This conclusion merely confirms the statement previously made by Le Count and Brooks, that many of the cases reported as sarcoma, angiosarcoma, lymphadenoma, etc., of the hypophysis are simply instances of hyperplasia or adenoma.

In the case about to be reported, the histologic changes found in the hypophysis, which was apparently unchanged upon gross examination are striking and confirmatory of the view advanced by Benda, that an increase in the chromophile cells is the distinctive anatomic lesion of the disease.

CLINICAL HISTORY.

C. H., aged 46, an unmarried German laborer, was admitted to the Cook County Hospital, in the service of Dr. J. B. Herrick, on the 6th of February, 1903. He complained of swelling of the feet, which he had first noticed two weeks before; dyspnœa upon exertion; a cough, dry and hacking in character; frequent headaches and pains in the lumbar region and extremities. The pains he described as pinching in character. Three weeks before entrance to the hospital he suddenly lost consciousness and asserted that he did not regain it for twenty-four hours. He had been subject to frequent attacks of vertigo. During the previous six years there had been a gradual but constant enlargement of the head and feet. No measurements had ever been taken, but the patient stated that six years ago he wore a 7¼ hat, and a number 9 shoe; whereas at this time he required a number 8 hat, and upwards of an 11 shoe. He had not worn gloves, and could not give any information concerning the increase in the size of his hands, but judged from appearances, that they also had become enlarged. The patient could give no history of mental changes, and relatives could not be found to supply such information.

Past and Personal History.—He had typhus fever when twenty years of age; malaria ten years ago. All venereal diseases were denied. He was moderately addicted to alcohol and tobacco.

Family History.—The father is dead, but the mother, two brothers and one sister are living and well. No member of the family, so far as the patient knew, ever suffered from a similar illness. There is no history of any giantism or disease resembling acromegaly in the family.

As the patient improved sufficiently to leave the hospital frequently, returning after a two or three weeks' absence, and the physical examinations in all the histories are the same, with the exception that they indicate a progress in the disease, the following account of his illness dealing with the significant symptoms only, has been abstracted from the numerous history sheets.

Physical Examination.—The patient is a well developed and well nourished, middle-aged man. His speech is thick and slow, skin dry and warm, facial expression sleepy and dull. The head is fairly well proportioned, but the lower portion of the face appears larger than the upper. The pupils react to light and accommodation, there is a lateral deviation of the left eye. The ophthalmoscopic examination was unsatisfactory, but as far as could be determined there were no changes in the fundus. Vision is slightly defective, and the patient experiences some diplopia. The pinna of each ear is increased in size; there is no defect in hearing. The nose is broad and flattened; the lips thickened and cyanotic; the teeth are well preserved, and there is no abnormal separation. The tongue is thick and tremulous, the palate high and arched. The chest is well formed, but there is to be noted an expansion of the lower thoracic zone, greater upon the left side. Relative dulness is noted over the sternum, corresponding to the sign described by Erb as indicating a persistent and large thymus.[23] Physical examination of the lungs elicits nothing abnormal. The right border of the heart extends 2 cm. to the right of the sternal line; the apex beat is found in the fifth intercostal space in the nipple line, and is diffuse; no thrills are palpable; a faint systolic murmur is heard over the mitral area, which is not transmitted into the axillary fossa. Over both the aortic and tricuspid areas systolic murmurs are heard, which are indistinct; that heard over the aortic area is not transmitted into the vessels of the neck. The second pulmonic tone is not accentuated.

The abdomen is large and flattened, and is prominent in the epigastric and hypochondriac regions. Hepatic dulness begins in the 4th intercostal space on the right side, flatness in the sixth. The anterior margin of the liver extends to the costal margin, but is not palpable; splenic dulness begins at the eighth rib in the mammillary line, and extends three fingers' breadth below the costal arch in the parasternal line; the organ is easily palpable and the crenations of the anterior margin are distinct; the kidneys are not palpable. Examination of a twenty-four hours specimen of urine: quantity 2200 cc.; alkaline reaction; sp. gr. 1013; no albumen or sugar; urea 1.15%; the sediment contains triple phosphates but no casts. Genitalia negative. The fingers of both hands are enlarged and spatulous, due to a diffuse thickening of all the tissues. The feet are likewise enlarged, especially the great toes. The markings of both the hands and the feet are exaggerated. Unfortunately, no measurements were made of the enlarged extremities, but the accompanying illustrations from X-ray pictures (Fig. 1 and Fig. 2) reveal the increase in the size of the bones. The increase in the size of the head and of the feet is indicated by the statements concerning the larger sizes of hats and shoes, which he now requires. The skin over the anteromedial surface of the right leg is pigmented; there is also a pigmented scar on the left leg. The osseous system presents no changes except those noted in the hands and feet, in which the bones are symmetrically enlarged. The lower jaw is apparently somewhat larger than normal, but does not protrude much beyond the upper. The spinal column shows no deformity. There are no exostoses about the joints.

While the physical condition of the patient improved some during his stay in the hospital, his mental condition grew progressively worse. He was often found in a stupor, from which he could be aroused only with difficulty. At other times he was delirious, and would talk wildly and incoherently. These stuporous and delirious states alternated. He was also the subject of attacks in which he lost consciousness, resembling the one previously described. During the night of April 19, 1903, he lost consciousness, and when examined the following morning its return was only partial and he was restless and groaning continually.

From the seventeenth to the twenty-fourth of January 1904, he had involuntary passages of urine and fæces. An examination of a twenty-four hours specimen of urine revealed, 550 cc.; amber color; acid reaction; sp. gr. 1020; a trace of albumen; no sugar; urea, 3%; the sediment contained erythrocytes, leucocytes and calcium oxalate crystals.

[23] This sign may be produced by a thickened sternum.

The patient improved slightly, and at his request left the hospital on the fourth of April 1904, to return two weeks later. No significant changes were noted during the subsequent stay of five weeks in the hospital. Following his discharge on May 23, 1904, he returned eight days later, in a semi-comatose condition, and although he could be aroused, he could give no history of himself, and seemed to be entirely unconscious of his surroundings. His pulse was strong and regular; the respiration Cheyne-Stokes in character. The results of the physical examination were the same as on previous occasions. Examinations of the blood by the usual methods revealed no important alterations. On the second of June, two days after admission to the hospital, a hemiplegia involving the right half of the face and body was noted. The course of the case from this time on was progressively downward. Defæcation and urination became involuntary; icterus developed, and the patient died at 5 a. m. on the eighth of June. Examination of the urine made on the day preceding death showed a sp. gr. of 1029, a small amount of albumen, no sugar or casts but some biliary pigments.

Autopsy.

At the post-mortem examination made by Dr. A. M. Stober, Resident Pathologist, the anatomic diagnosis was as follows: Cerebral embolism with softening and secondary hemorrhage; chronic fibrous endocarditis of the mitral, tricuspid and aortic valves; hypertrophy of the heart; fibrous pleuritis of the right side; œdema of both lungs and hemorrhagic infarction (left lower lobe); cirrhosis of the liver; passive congestion of the kidneys and spleen; tuberculosis of the peribronchial lymph nodes and acromegalic osseous hypertrophy.

The following descriptions from the record are of interest.

"The thyroid gland weighs 30 g., and is of normal shape and consistency. Upon section, the gland appears normal.

"The heart weighs 500 g., and has no abnormal external markings. The tricuspid orifice easily admits five fingers, and the mitral four. Sclerotic plaques are found upon both valves. The aortic and pulmonic valves are competent to the water test. The root of the aorta presents some areas of sclerosis, the right ventricular wall measures 7 mm. in thickness and the left 22 mm. The coronary vessels show no changes. The foramen ovale is closed, and the thoracic and abdominal aorta appear normal. The left lung weighs 1240 g. It floats low in the water, and has a middle lobe. The upper lobe is crepitant throughout with the exception of a small area near the apex, where there is an old scar. Crepitation can be elicited in the lower lobe anteriorly, but below and posteriorly crepitation is diminished, and in some places absent. Upon section a frothy, bloody fluid escapes, and in the region where crepitation is diminished is found a large hemorrhagic area. The middle lobe of the left side is normal, and the pleural cavity is free. The right pleural cavity is obliterated by heavy fibrous adhesions. The right lung presents nothing abnormal.

"The liver weighs 1080 g. Its external surface is irregular, and upon section the surface appears broken up into islands of liver tissue separated from each other by shining bands of connective tissue. The bile ducts are patent and normal.

"The spleen weighs 1169 g., its capsule is thickened. Upon section considerable bloody fluid exudes. The Malpighian bodies show distinctly, and an increase in the amount of connective tissue is evident.

"Together, the kidneys weigh 540 g. The right kidney measures 15 by 6.5 by 5.5 cm. Externally it is smooth and the capsule strips easily. The cortical markings are distinct. The cortex measuring 1 cm., the pyramids 1.5 cm.; considerable bloody fluid escapes from the kidney tissue. A similar description answers for the left kidney, with the exception that it is larger and paler. The pelvis of each kidney is unchanged. The bladder is full of urine, and the mucous membrane covering the trigone contains numerous engorged capillaries. The seminal vesicles and testicles appear normal.

"Except for a slight diffuse thickening, the bones of the skull show no changes. On removal of the calvarium considerable blood stained fluid escapes; the dura appears normal. On removing the dura the left half of the cerebrum appears smaller than the right and there is considerable blood over its upper surface; an incision into the left ventricle parallel to the median fissure and 2 cm. on the left, from the occipital lobe behind to the frontal lobe in front, extends through an area of hemorrhage and considerable blood is present in the ventricle."

Since the brain was soft it was placed in 10 per cent formalin without further examination; after hardening, frontal sections were made at intervals of from 2 to 3 cm., and the following record made.

"When the brain is viewed as a whole after placing the sections together, two striking changes are noticed; (1) a narrowing of the left occipital lobe; 6 cm. from the occipital pole its circumference is 12.5 cm., whereas the right at a similar point measures 23 cm. in circumference. This reduction in size is mainly in the vertical dimension, but also slightly in the lateral. (2) The upper surface of the left hemisphere except in the anterior part of the frontal lobe, shows a marked diminution in the size of the gyri which are sunken and separated by abnormally wide sulci and these are filled with clotted blood. These changes are perhaps most marked in the post-central and superior parietal gyri.

"In the hemisphere 1 cm., from the median line there is a rent which slopes outward to the roof of the lateral ventricle so that where it opens into the ventricle it is 2 cm. from the median line. This tear connecting the ventricle with the meningeal cavity is lined by dark necrotic brain tissue; its walls are the seat of many minute hemorrhages; the necrosis is superficial extending only from the surface of the tear 3 mm., on an average.

"On examining the sections of the brain there are no changes found in the first two, each made 3 cm. from the frontal pole. In the section 6 cm. from the frontal pole a small amount of clotted blood is found in the right lateral ventricle. Examination of the section 2.5 cm., posterior to the previous, shows a lessening, amounting approximately to 1 mm. in the thickness of the cortex of the left hemisphere from the mesial to the Sylvian fissures, when this half is compared with the right side. The pia dipping into the fissure of Rolando is ecchymotic, and in this section there is no blood in the right ventricle. In the next section (see Fig. 3) 3 cm. behind, the narrowing of the gyri is very marked and the sulci between the mesial and Sylvian fissures are both deep and wide. The tear found on the external surface extends 3 cm. forward from this section and in this plane the white substance of the superior and inferior parietal lobes is destroyed and partially replaced by blood.

"In the next plane of sectioning, 7 cm. in front of the occipital pole, the left occipital lobe appears very much smaller than the right and the right posterior horn is filled with blood clot; these changes, a small left occipital lobe and filling of the right posterior horn with clotted blood to its termination are the only changes revealed in the remaining sections. The right hemisphere weighs 550 g., the left 515 g. Posterior to the section 7 cm., from the occipital pole, the left hemisphere weighs 70 g. and the right 110 g."

The anatomic changes in the remaining organs do not demand a detailed description.

HISTOLOGIC EXAMINATION.

The acini of the thyroid gland are filled with colloid material, and the interacinar connective tissue seems to be slightly increased, but otherwise the gland may be said to show no pathologic changes.

In the heart muscle the interstitial tissue is not increased in amount. There is some yellowish pigmentation of the poles of the muscle cells.

In a section through the hemorrhagic area in the lower lobe of the left lung, the alveoli are seen to be so filled with blood that the appearance of alveolar structure is lost. In the alveoli bordering upon this area a granular material (coagulated albumen?) is seen; the respiratory epithelium is loosened in places, and the interstitial tissue appears swollen. Similar granular material is found in the alveoli of the right lung. The external surface of this lung is covered by a recently organized layer of connective tissue measuring about 1 mm. in thickness; immediately adjacent to the lung, round cells are found in abundance, also newly formed capillaries.

Liver.—The liver lobules are surrounded by a newly-formed connective tissue, which extends some distance into the lobule. There is no increase in the number of bile capillaries. The liver cells appear to be compressed, but for the greater part they appear to be quite normal.

Kidneys.—The glomeruli do not fill their capsules, the vessels of the capillary loops are filled with blood; the lining of the capsule is unchanged. The cells lining the secreting tubules appear swollen, but stain well. The lumina of the tubules are free; the interstitial tissue is not increased.

Spleen.—The capsule of this organ and its trabeculæ are greatly thickened. The organ is congested, red blood corpuscles being diffused throughout the splenic tissue. No other pathological changes are to be noted.

Before describing the histologic changes in the hypophysis in this case, a brief consideration of the various theories concerning the nature and significance of the different kind of cells found in the anterior lobe of the normal gland would seem to be appropriate.

But little space is devoted in text books on histology to the pituitary body. Böhm and Davidoff[24] describe its anterior lobe as being surrounded by a connective tissue capsule, within which are found variously shaped alveoli or follicles, or again, columns and trabeculæ of cells, which are separated by connective tissue, supporting blood vessels. Mention is made of two kinds of cells, which can be differentiated by their staining reactions, size and structure. One variety, round or oval in shape, with a nucleus centrally placed, has a protoplasm which contains coarse granules, possessing an affinity for acid dyes; these are the chromophile cells. The other variety is cubic or columnar in shape, with a nucleus placed near the base of the cell; their protoplasm is faintly granular, and has an affinity for basic dyes; these are the chief cells.

Szymonowicz[25] describes two kinds of cells, and states that some authors regard the difference in appearance as due to post-mortem or to functional changes.

[24] Böhm and Davidoff: Text-book of Histology (edited and transl. by Huber). 1904.

[25] Szymonowicz: A Text-book of Histology and Microscopic Anatomy of the human body. 1902.

Flesch[26] and Dostojewsky[27] were the first to describe in the glandular lobe of the hypophysis two kinds of cells which they called chromophile and chromophobe cells. According to these observers the cells of the first variety are coarsely granular, measuring from 15 to 25μ in diameter. They stain readily with eosin, osmic acid and indigo-carmin; and in fresh unstained preparations appear darker than the chromophobe cells.

Subsequently Schönemann[28] divided these chromophile cells according to their reactions to hematoxylin and eosin, into the cyanophile and eosinophile cells. The former stain a light blue with hematoxylin, whereas the latter take the ordinary eosin stain. The chromophobe cells are smaller than the chromophile; do not stain with eosin and osmic acid; but present, after the use of these stains, a light yellowish tint.

In addition to these two kinds of cells Rogowitch[29] described groups of nuclei surrounded by a scanty protoplasm, which he regarded as embryonal or undifferentiated tissue.

Saint-Rèmy[30] in 1892, from results obtained by the use of the Altmann granule technic, suggested that all these types of cells are merely functional stages of one another, and his conclusions have been supported by Claus and van der Stricht[31] and Benda. Benda[32] using special fixing and staining methods, was able to follow satisfactorily the transitional stages from the empty chromophobe to the loaded eosinophile cell and described the following types of cells. A small cell with irregular clear protoplasmic body containing few granules; a larger round cell, the body of which is so filled with granules that only a small zone about the nucleus and a light area "*heller Hof*" containing the centrosome remain free; and, finally, a large irregular cell, containing isolated masses of stainable granules. In this last variety vacuoles are found which have been regarded by many investigators as secretion vacuoles, but Benda has demonstrated by the examination of fresh specimens and the use of Sudan III and osmic acid that they contain fat. His conclusions concerning the significance of these different types of cells are stated as follows: "I may conclude from the characteristics of these cells, that the small cells with few granules represent the indifferent embryonal forms capable of multiplying, that the accumulation of granules in the dark cells indicates the highest point of functional

[26] Flesch, M.: Versamml. deutscher Naturforscher und Ärzte in Magdeburg, 1884, 195-196.

[27] Dostojewsky: Über den Bau der Vorderlappen des Hirnanhanges. Arch. f. Mikr. Anat., Bonn, 1886, XXVI, 592-598.

[28] Schönemann, A.: Hypophysis und Thyroidea. Virch. Arch., Berl., 1892, CXXIX, 310-336.

[29] Rogowitch, N.: Die Veränderungen der Hypophyse nach Entfernung der Schilddrüse. Ziegler's Beiträge, 1889, IV, 455-469.

[30] Saint-Rèmy, G.: Contribution à l'histologie de l'hypophyse. Arch. de Biologie, 1892, XII, 425.

[31] Claus, A., and van der Stricht, O.: Contribution à l'etude anatomique et clinique de l'acromègalie. Ann. et Bull. de la Soc. de Méd. de Gand., 1893, 71.

[32] Benda, C.: Beiträge zur normalen und pathologischen Histologie der menschlichen Hypophysis cerebri. Berl. klin. Wchnschr., 1900, XXXVII, 1205-1210.

activity, and that, finally, the large cells with few granules result from a temporary or permanent cessation of function."

This theory that these different varieties of cells are merely functional stages of one another passed unchallenged for twelve years. Scaffidi[33] in a recent article, takes an opposite view. He has described two distinct and functionally independent types of cells. In his study he used acid hematoxylin as a nuclear stain, and a mixture consisting of two parts of a 2% watery solution of orange G., and three parts of a 1% solution of acid fuchsin, as a cytoplasmic stain; the two varieties of cells we may refer to conveniently as the "orange G. cell" and the "fuchsin cell." The former, measuring about 12μ in diameter, has a cytoplasm, which contains small round granules and stains readily with orange G.; its violet-dyed nucleus sharply differentiated from the yellowish cytoplasm is small, oval and fairly rich in chromatin granules. On the other hand, the "fuchsin cell" contains large, coarse, granules, which are irregular in form and unequal in size. Its nucleus is large and vesicular, and the chromatin network is loose enclosing large spaces. There are found almost constantly within the meshes of the chromatin network granular masses which stain with fuchsin. No similar granules are ever found in the nucleus of the orange G. cell.

According to Scaffidi, then, there are within the anterior lobe of the hypophysis two functionally distinct varieties of cells, each producing a specific substance; the products of both together form the secretion of the gland. The cyanophile cell of Schönemann is to be regarded as a fuchsin cell in the advanced stages of elimination, and the groups of nuclei surrounded by a scanty protoplasm, as the end phase of secretion. Further, cells of the orange G. type are found, which differ in their histologic picture, according to the stage of secretion encountered. Scaffidi's work is apparently confirmed by the studies of Schäfer and Vincent[34] who have isolated from extracts of the glandular lobe of the hypophysis, two distinct substances, one of which depresses the nervous system, whereas the other stimulates, and at the same time raises blood-pressure.

At the present time it is impossible to state which view concerning the nature of the cells of the hypophysis is correct. The theory advanced by Saint-Rèmy and supported by Claus, van der Stricht and Benda, that they are merely functional stages of one another, demands as much consideration as the theory of Scaffidi, who regards them as independent forms of cells. Further investigation is needed to determine these questions.

Pathologically, it makes little difference which view we accept, for in either case the presence of an unusually large number of cells heavily loaded with granules indicates a gland which is functionally more active than normal.

[33] Scaffidi, V.: Uber den feineren Bau und die Funktion der Hypophysis des Menschen. Arch. f. Mikr. Anat., Bonn., 1904, LXIV, 235-257.

[34] Schäfer and Vincent: The physiological Effects of Extracts of the Pituitary Body. J. Physiol., Lond. and Cambridge, 1899, XXV, 87-97.

The relative proportion of the chromophobe to the chromophile cells varies with the age of the individual. Erdheim has called attention to the predominance of the chromophobe cells in the fœtus, only isolated chromophile cells being found.[35]

The chromophile cells increase gradually, but constantly, up to the middle age, at this time, being equal in number to the chromophobe cells; after middle age the chromophile cells gradually decrease, so that in old age the relation between the two elements approaches more nearly that found in the fœtus. In both varieties of chromophile cells fat is found. The fatty deposits increase with age, reaching their maximum in old age. Virchow states that a greater number of the cells of the glandular lobe undergo a fatty metamorphosis with advancing age, and that the fat gives to the extracts of the gland the appearance of the "milky fluid," described by Santorini. Occasionally, a tumor of the hypophysis is described as resembling softened brain tissue. This appearance probably depends upon post-mortem changes in the gland, with the expression of this "milky fluid."

Returning now to the case of acromegaly which forms the basis of this article, the hypophysis appeared normal macroscopically. Sections were taken from different parts of the gland, fixed in Zenker's fluid, and 5% formalin, imbedded in paraffin following the ordinary technic, cut and mounted serially. Different stains were used, the most satisfactory being hematoxylin with eosin or Congo-red, iron-hematoxylin and hematoxylin according to Bensley's formula.

The histological changes correspond in many ways to the description given by Shattock, Brooks, Benda, Mitchell and Le Count, and others, of tumors of the hypophysis, associated with acromegaly; they concern the character, number, and arrangement of the cellular elements. The stroma is reduced in amount. In the normal hypophysis there is a connective tissue supporting blood vessels, which surround the follicles and forms a basement membrane for the cells. In this hypophysis there is very little stroma, and the cells rest directly upon the endothelial walls of the capillaries, being irregularly grouped together in the intercapillary spaces.

Very few of the chromophobe and cyanophile cells can be found, and where present, they are grouped about the boundary zone between the nervous and glandular lobes. Two kinds of cells are easily distinguishable, a small round cell, with a small compact nucleus, and a large polyhedral cell, with a large vesicular nucleus and loose chromatin network. The former corresponds probably to the orange G. cell of Scaffidi, and the latter to the so-called fuchsin cell. It is impossible with the Congo-red and eosin stains to differentiate the granules in the cells, for the cytoplasm takes a homogeneous stain; but with the iron-hematoxylin stain the granules may be seen in the cells which are not too heavily loaded. The granules are small and regular in outline. Many of the cells, however, are so full of granules, that these granules appear to be coalescent forming such a mass in the cytoplasm, that single granules cannot be differentiated. In Fig. 4 a number of the large polyhedral cells may be seen. Some contain two or three nuclei, but these multinuclear cells cannot be regarded as pathological, as they are often found in the normal hypophysis. No karyokinetic figures occur in these cells. Some also are vacuolated, but the vacuolation is not in excess of the normal. These chromophile cells have an atypical arrangement

[35] The latter must be differentiated early, however, for I have found eosinophile cells in the hypophysis of 4.5 cm. fœtal pig.

in that the follicles seem to have fused, and the cells are irregularly grouped.

All the changes in the gland, the great excess of the highly functionating chromophile elements, their irregular disposition, and the lessened amount of stroma, are indicative of excessive function. I have had the opportunity of examining sections of the hypophyses of other cases of acromegaly, and the histologic change, an hyperplasia or increase of glandular cells of a particular type, corresponds closely to the one under consideration.

The hypophyses from several post-mortem examinations taken at random were used as controls, and a brief description of these will suffice to indicate the peculiar and distinctive differences presented by the hypophysis in acromegaly.

Female, aged 50; clinical diagnosis: Exophthalmic goitre. The stroma is increased in amount; the alveoli are reduced in size, and although the chromophile elements are normal in number, they are smaller and more vacuolated than in the normal gland. No abnormal pigment is present. I think that one would be justified in saying that this gland was not functioning normally.

The vicarious relation supposed to exist between the thyroid gland and the glandular lobe of the hypophysis, make the examination of the latter important in Graves' disease. Benda has examined the pituitary glands of three cases in which death was due to exophthalmic goitre; in two the hypophyses were small and indurated, in the third it was macroscopically normal. The alveoli in the former were found, upon microscopical examination, to be small and to contain few chromophile elements; the cells were atrophic, vacuolated and contained a dark brown pigment. Some sections from the gland which showed no gross changes, presented a normal histologic picture, and in others the same changes occurred as in the atrophic glands.

The changes in these glands are of interest in connection with the alterations in shape of the fingers in acromegaly and in patients suffering from Graves' disease. In the latter the delicately pointed fingers which have been compared by Revilliod to the fingers of the Madonnas of Raphael and Perugino, are in marked contrast to the blunt fingers of acromegaly.

Male, aged 28. Anatomic diagnosis: Syphilitic endarteritis, cerebral thrombosis and softening. The chromophile cells predominate in the central part of the gland and peripherally the chromophobe are found in excess, only isolated chromophile elements being found here. The eosinophile cells are of normal size, but are not vacuolated, as in the preceding case. The capillaries are filled with erythrocytes, but this hyperemia cannot be regarded as pathological.

Male, aged 44. Clinical diagnosis: Pernicious amæmia. The chromophobe and chromophile cells are about equally divided. The eosinophile cells take a lighter stain than usual, and the granules are grouped together. The cells are vacuolated, but not to the extent one might expect in pernicious anæmia. The stroma is normal and the capillaries are empty.

Male, aged 60. Clinical diagnosis: Tabes dorsalis and cystitis. The alveoli are small; the chromophobe and chromophile elements are equally distributed and no other changes are found.

Male, aged 42. Anatomic diagnosis: Tuberculous meningitis. Several large colloid cysts occur near the nervous lobe; these cannot be considered pathological, for they are often present in the normal gland. The chromophobe and chromophile elements are about equal in number, and show no changes.

Still-born infant. The glandular lobe of the hypophysis consists of well-formed columns of cells separated from each other by a scanty stroma. The chromophobe elements greatly exceed in number the chromophile, only isolated groups of the latter being found.[36] Occasionally cells are found, the protoplasm of which takes a light stain with Congo-red. These cells are probably transitional stages from the chromophobe to the chromophile.

Male, aged 85. Clinical diagnosis: Senile dementia. This gland resembles the preceding. The chromphobe elements are in excess of the chromophile. It is well-known that in old age the latter cells decrease in number. The gland resembles somewhat that of the new-born, with the exception that the cells are larger, and contain more fat. The stroma is more developed than in the still-born infant.

In none of these hypophyses, therefore, was there any indication of the hyperplastic process, which, apparently is the fundamental and characteristic change in acromegaly, and which is so distinctive that the pathologist may make an anatomic diagnosis of acromegaly in cases which are doubtful from their clinical features, and thus differentiate acromegaly from other closely allied conditions. We might properly assume that if the disease in this case had pursued its usual clinical course and had not been interrupted by death from cerebral embolism and a terminal hemorrhage, the gland would have become enlarged; perhaps, incidentally, the seat of a tumor-like hyperplasia of cells which are found normally in the hypophysis.

Sarcoma of the hypophysis is the lesion most frequently described as being associated with acromegaly. Sternberg[37] states that adenomas have been described seven times, large-cell sarcoma six times, and other forms of sarcoma five times. Among the forty-seven cases collected by Furnivall, in which the hypophysis was enlarged, some variety of sarcoma was noted in fifteen. However, all of these cases ran a longer clinical course than is usual with sarcoma developing in other parts of the body, and no metastatic growths were reported although occasionally direct extension of the so-called tumor cells to adjacent structures was observed.

According to Sternberg: "In all cases of acute progress—and only these—a true sarcoma of the hypophysis is present." These acute cases, few of which are reported, terminate fatally in three or four years. Although they resemble in length the clinical course of sarcoma of other organs, they differ essentially in some particulars. Rolleston,[38] who has observed and reported one of the acute cases, thus expresses his belief that there are certain differences between the so-called sarcoma of the hypophysis and the ordinary sarcoma encountered elsewhere: "The course of the disease (three years), which

[36] Mention has already been made of Erdheim's work, in which he finds that few chromophile elements are present at birth, but that they increase gradually, but constantly up to middle age.

[37] Sternberg, M.: Die Akromegalie, Nothnagel's Specielle Pathologie und Therapie, 1903, VII, 30.

[38] Rolleston, H. D.: A case of acute Acromegaly due to Sarcoma of the pituitary body. Tr. Path. Soc., Lond., 1898, XLIX, 237-242.

is comparatively long for malignant tumors, suggests either that some change has taken place in the nature of the pituitary tumor, such as supervention of a more malignant and rapid type of growth in the later stages of the disease, or that pituitary sarcoma is less malignant than sarcoma in general." It is hard to conceive why sarcoma of the hypophysis should be less malignant than sarcoma of other organs. Although, in Rolleston's case, the tumor had extended into the third ventricle, the optic nerve and the petrous portion of the temporal bone, no metastic growths were reported in distant viscera. In such a gland as the hypophysis, with large and numerous capillaries it would seem that abundant opportunity would be afforded for transportation of tumor cells, and that secondary growths in distant parts would result.

Relative to the nature of many of these reported cases of sarcoma, Le Count[39] makes the following pertinent observation: "If these growths were examples of a tumor as malignant as we know round-cell sarcoma to be, why do we not have cases of metastasis? Certainly not from lack of adjacent blood vessels. And why are the phenomena of cell division so common to sarcoma entirely lacking in the histologic descriptions? It must be conceded that hyperplasia and not true tumor is the condition of the hypophysis in instances where large solid growths have been found." That mistakes in diagnosis of the lesions of the hypophysis in cases of acromegaly might arise, is readily understood when the atypical structure of the gland is considered. Benda has already emphasized this point. In examining sections of an adenoma of the hypophysis he found that the histologic changes varied; in some fields resembling a typical adenoma; in others a carcinoma, and in still others an angio-sarcoma. Brooks also mentions the possibility of such errors in diagnosis and in one case temporarily mistook a simple hyperplasia for a round-cell sarcoma. For these reasons, the long clinical course of acromegaly, the absence of metastatic growths, and the fact that errors may occur in a failure to recognize the process, we are justified in believing that the reported tumors of the hypophysis, in this disease, are instances of hyperplasia.

[39] Mitchell, L. J., and Le Count, E. R.: Report of a Necropsy in a Case of Acromegaly with a critical Review of the recorded Pathologic Anatomy. N. Y. M. J., 1899, LXIX, 517, 556, 595.

In this connection Tamburini's[40] suggestions that acromegaly is dependent upon excessive function of the gland is highly important. As yet no cases of undoubted acromegaly have been reported in which changes in the gland were absent upon both gross and microscopic examination; and in those instances where necrosis and softening (probably post-mortem), sclerosis, colloid degeneration, etc., have been found no mention is made of the relation between chromophile and chromophobe elements. Experimental removal of this gland, its destruction by neoplasm, infectious granulomata, and aneurysm as previously stated do not produce the disease, so that it seems proper to assume that acromegaly is not dependent upon an abolished or lessened function of the hypophysis.

On the contrary, all the facts seem to point to an increased function of the gland as the essential etiological factor, and henceforth no report should be considered complete which does not take into consideration the character, number and disposition of the chromophile elements, for, as Brooks[41] aptly states, "An overgrowth of the hypophyseal cells mainly composed of the chromophile cells might not be accompanied with the grosser degrees of enlargement, and still be of great significance in acromegalia."

This case is noteworthy in that: 1. It came to autopsy at an unusually early stage of acromegaly, the usual clinical course of a benign or chronic case having been interrupted by death due to cerebral embolism and secondary hemorrhage. 2. The hypophysis appeared normal upon gross examination, but microscopic examination revealed a hyperplasia, especially of the chromophile cells, which is confirmatory of the theory that acromegaly is caused by excessive function of the glandular elements of the anterior lobe of the hypophysis.

I wish to express my thanks to Dr. E. R. Le Count for the material and valuable advice, to Dr. L. F. Barker for valuable suggestions and to Mr. L. H. Wilder for the accompanying drawing of a section of the hypophysis.

[40] Tamburini: Quoted by Mitchell and Le Count.

[41] Brooks, Harlow: Acromegalia. Archiv of Neur. and Psychopath., 1898, I, 485-652.

STUDIES IN TYPHOID FEVER.

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FIG. 1.—Reproduction of an X-ray picture of the left hand viewed from the dorsal surface. Slight enlargement of the distal row of carpal bones and the heads of the metacarpal bones is evident. The muscular attachments are rougher than normal. The osteophytic shadows about the ungual phalanges are normal.



FIG. 2.—Reproduction of an X-ray picture of the left foot viewed from the plantar surface. The metatarsal bone of the great toe is larger than normal. Nothing abnormal is seen in the remaining bones. The distal phalanges do not show.

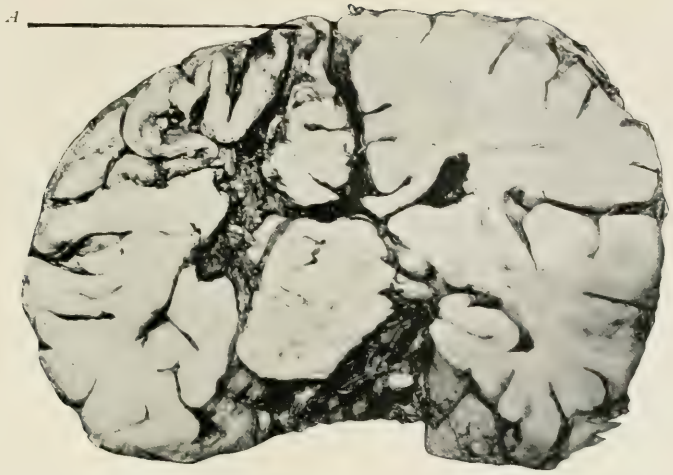


FIG. 3.—Posterior view of the cerebrum in a frontal section 7 cms. from the occipital pole. The gyri on the left side are greatly reduced in width and the sulci are wide. At *A* rupture occurred.

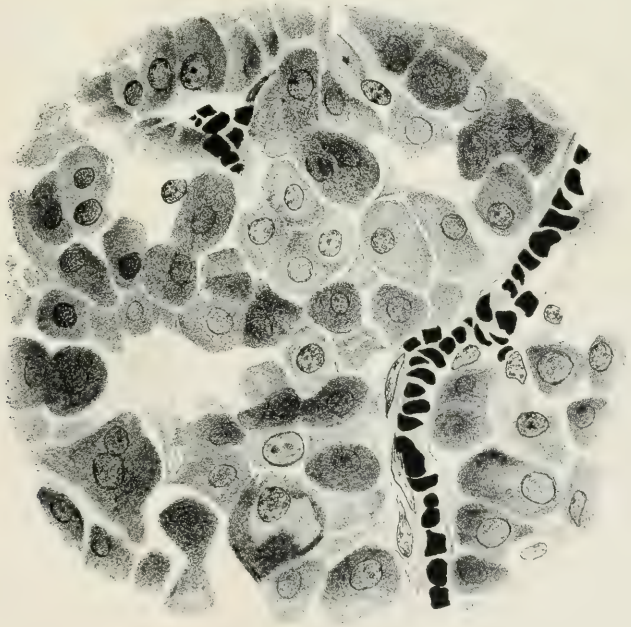


FIG. 4.—Section of the hypophysis: The stroma is reduced in amount, the cells resting directly upon the endothelial walls of the capillaries. The cells are of the chromophile type and are grouped in the inter-capillary spaces, the follicles having fused. In some cells two nuclei are found, but these cannot be regarded as pathological, for in the normal gland cells containing two nuclei are frequently found. Stained with iron-hæmatoxylin. (Leitz, Obj. 12. Ocular, No. 4.)

THE HISTORY OF THE CIRCULATION OF THE BLOOD—CONTRIBUTIONS OF THE ITALIAN ANATOMISTS AND PHYSIOLOGISTS—THEIR BEARING UPON THE DISCOVERY BY HARVEY.

By John C. Hemmeter, Phil. D., M. D., etc.

Professor of Physiology and Clinical Medicine, University of Maryland, Baltimore.

A very curious impression is made upon the objective investigator to see the scientific judgment obscured by ill-guided patriotism. No less than four monuments have been erected in three different countries to perpetuate the memory of four different discoverers of the circulation of the blood. The Spaniards regard Michael Servetus, born in Villanueva in 1511, as the discoverer of the circulation, and have erected a monument in the Museo Anthropologico at Madrid. The Italians have three men to whom the title to this discovery is accredited with more or less historic and scientific correctness, namely: Matheus Realdus Colombus, born at Cremona in 1516; Carlo Ruini, of Bologna;[1] Andreas Cesalpinus, born at Arrago in 1519. Monuments have been erected to Carlo Ruini at Bologna and to Andreas Cesalpinus at Pisa and Rome. William Harvey has been honored by a monument in London erected by the Sydenham Society, a second at Hempstead, and a third at Folkstone. This makes five discoverers in all, but there is one more. The French have claimed the discovery of the circulation of the blood, and their discoverer is that incomparable satyric François Rabelais, and this assertion is made by no less than Paquelin.[2] But a critical study of the passages from Rabelais, which Paquelin cites, proves that the alleged French discoverer brings nothing new, nothing which was not already stated by Galen, that he nowhere mentions dissections or vivisections as basis for his claims.

The department of physiology which was most fatally retarded in its progress by a defective knowledge of the ancients is that concerning the circulation of the blood. In the Lane lectures, delivered at Cooper Medical College, San Francisco, in 1900, Sir Michael Foster has given us an admirable review of the history of the circulation of the blood. These lectures constitute a most scholarly and inspiring addition to our knowledge of the subject. The first and second chapters of this book treat of the circulation, especially the second chapter. The first chapter does not treat of the circulation directly, but of Vesalius, his forerunners and followers. In narrating the contributions of the Italian physiologists and anatomists, there is this difference between the tenor and spirit of presentation by Foster, and that by Spanish and Italian medical historians. Foster leaves us under the impression that the Italian physiologists and anatomists made no contributions or discoveries of enduring excellence or genuine scientific merit, whereas the Italian historians[3] make every effort to convince us that the work of their fellow-countrymen constituted solid building blocks in the architecture of physiology; that their conclusions were based upon precise and accurate observations and experiment, as far as such were possible in those days. In order to judge with what justification the claims of the Italian authors are made, and also to judge of the critical conservatism and broad experience of Sir Michael Foster, a brief and critical review of the main contributions of the more renowned Italian workers in physiology and anatomy, and of Harvey, becomes indispensable.

In the "*Deutsche Rundschau,*" Helmholtz[4] credits poetic genius with the power of reviving long-past historic personages and transactions, and clothing historic characters not only with flesh and bone and garments, but with exactly portraying their psychic individuality and real personality. At the same time there is also an exact probing of the plausibility of the existence of certain characters. We can see this in the Thalmud connoisseurs, some of whom, of Jewish creed, have denied that Job and Jonah ever existed, and upheld other characters of the Old Testament as real personages. One has to be a very thorough, patient, persistent, and judicial student of any great historic character in order to successfully think oneself into the life and work and individuality of the person.

This is true in the study of the lives of Michael Servetus, Vesalius, Harvey, and others; it is not sufficient to read their history,—one must repeatedly sink one's psychic self into the life and period of the personage to be studied. Medical history writing, unless the writer and student has sunk his soul into the soul of the character to be studied, unless he has become part and parcel of the life and work, individuality, and even the social, scientific, religious, and political condi-

[1] Book on Anatomy and Diseases of the Horse, published in 1598, in which Ruini gives the unmistakable evidence that he had grasped the action of the cardiac valves.

[2] Revue de Litér médic, 1878, p. 499.

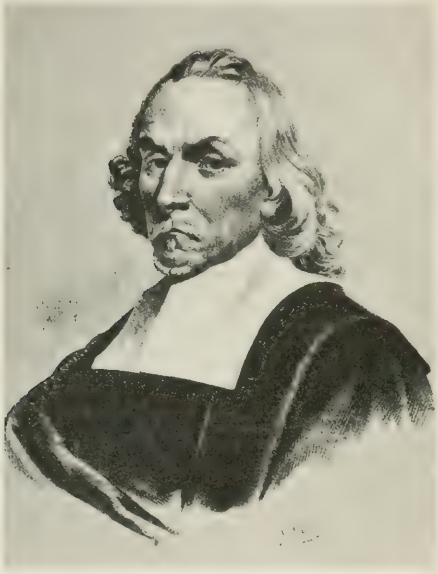
[3] See Luigi Luciani, Physiology of Man, at present being translated into German by Baglioni and Winterstein: § G. Ceradini. Ricerche storico-critiche intorno alla scoperta della circolazione del sangue, Milano, Fratelli Rechiedei, editori, 1876. Difesa della mia Memoria intorno alla scoperta della circolazione, contro l'assalto dei signori H. Toll in teologo in Magdeburg, e W. Preyer fisiologo in Jena. Con qualche nuovo appunto circa la storia della scoperta Medesima. Genova, tip del R. Instituto Sordo-muti, 1876.

For further literature on this subject see list at end of this article: "Literature on the History of the Discovery of the Circulation of the Blood."

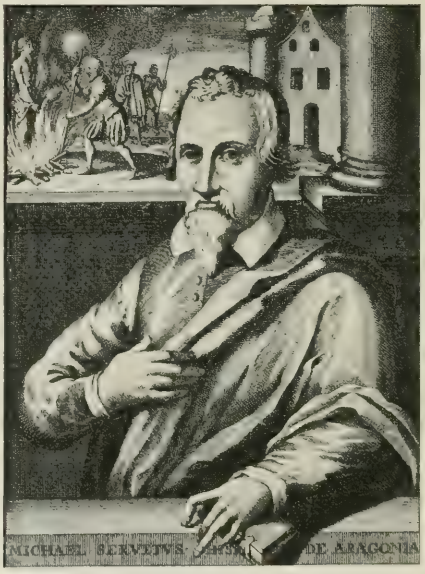
[4] Goethe's Wissenschaftliche Thätigkeit.

tion under which that character developed and produced his results, has little value for an analytical mind.

In order to present a medical character justly and as correctly as possible, it is necessary to become a connoisseur of that character, and all the conditions influencing and surrounding him. We thus are even now able to recognize specialists on Galen, Vesalius, Servetus, Harvey, just as there are music lovers who are specialists of the compositions of Rameau, Paganini, Bach, Mozart, Beethoven, Chopin. Musical notes as printed are only the skeleton of music. Note-reading and mechanical technique will never make an artistic player. "He is not a correct interpreter of a composer until he puts his soul into it."



Guillaume Harvey, 1578-1657 A. D.



Michael Servetus, 1511-1553 A. D.

This identification of the subjective powers of an artist with the work and musical nature of the composer, resurrects the composer before the mind's ear and eye of the performing artist. He begins to realize the subjective and objective peculiarities and becomes familiar with the train of thought and musical feeling that prompted the composition.

Similarly the mere reading of biographies and personal histories of distinguished anatomists and physiologists, without a calm, self-possessed and patient analysis of all the collateral sources of information, will not give a picture of life-like distinctness. It is like playing the notes of a composer mechanically in the absence of a wide reach of innate musical gifts. What is needed in medical biography as well as in the reproduction of classical music is the focusing of the entire mental energy of the writer upon the historic or musical problems in hand,—reading the literature in its original sources, and not from abstracts or quotations second-hand, and eventually, if possible, to combine the facts and data from all sources of information into an organic life-like whole, making the character and his times comprehensible to our modern methods of thinking.

The history of the discovery of the circulation of the blood begins with Galen (125-201 A. D.), who by his vivisections exposed the error of the Alexandrine school under Erasistratus (300 B. C.), who held that the left portion of the heart and the arteries were empty and that they, communicating by means of the small bronchi with the arteria aspera (trachea) served to convey the spirit of life (pneuma) to the various parts of the body, to animate them and that the veins alone contained blood with which to nourish the entire body.

Galen showed that one need only to prick any artery or the left portion of the heart of a living mammal, in order to see blood gushing forth, which, in contrast with venous blood, was vaporous, thin, and "genuine," and which therefore consisted of a mixture of blood with the air inhaled in the lungs: "mixtum quid ex ambobus."

According to Galen the left side of the heart is the center of the arteries, which through systole drives the *air-containing* (ærated?) blood (sanguis spirituosus) into all the organs, to animate them. The center of the veins on the other hand is the liver, from which the nourishing blood (sanguis nutritivus) is carried to all parts of the body by a kind of attractive and selective force. The blood from the right side of the

heart, from the cava inferior, goes for the most part into the left ventricle, through the pores of the septum (which Galen assumes, although he declares them to be invisible). In the left ventricle it becomes "spirituous" through mixture with pneuma, and through the aorta it is distributed over the entire body. However, a small portion of the blood contained in the right ventricle passes through the vena arteriosa (arteria pulmonaris) and then by way of the arteria venosa (venæ pulmonales) reaches the left ventricle.

Galen therefore had a notion, although imperfect, of the circulation of the blood through the lungs, and he knew that the venous vessels anastomose with the arterial ones, since he also had observed, that an animal might bleed to death from a single artery. One point, however, in Galen's theory might lead some critics astray in the explanation of the text. Galen assumed that the blood of the arteria venosa (venæ pulmonales) flowed back into the lungs at each systole (through a sort of physiological insufficiency of the bicuspid or mitral valve), in order to exhale here the "soot" formed in the blood. Thus he assigned to the arteria venosa a double, and that an opposite, function, that is to say, first of conveying the reanimated blood from the lungs to the heart, and then again of conveying a portion of the same with the "soot"[5] from the heart to the lungs. Similarly Galen assigned to the vena portæ a double function, in that he assumed that during digestion it conveyed the chyle to the liver, and when the intestinal canal is empty, it conveys the blood from the liver to the intestinal canal.

Certainly the two errors of the permeability of the septum and the systolic reflux dim, not a little, the splendor of Galen's theory of the lesser circulation; nevertheless it cannot be denied that Galen was the first to have a conception of the same, a fact which was recognized (long before G. Ceradini again drew the attention of investigators to it) by representative interpreters such as Harvey, Haller, Douglas, Maurocordato, and Senac, who referred especially to a passage in the 10th chapter of Book VI, "De usu partium," in crediting Galen with a conception of the respiratory circulation.

Let us now see who first corrected and completed the theory of Galen, by the rejection of the assumption of the permeability of the cardiac septum, and by the determination of the fact that not only a part, but all the blood driven out from the right ventricle reaches the left ventricle by anastomoses of the pulmonary vessels.

In the year 1553 the Spanish physician and theologian Michele Reves (better known by the anagram of Serveto or Servetus) published his book entitled, "Christianismi restitutio," which at the instance of Calvin resulted in the author's condemnation and death at the stake, in October of the same year, at Geneva. In this book about a theological matter (there are only two copies extant, since the greater number were burned, first at Vienne (Dauphiné) together with the effigy of the author, and then in Geneva simultaneously with the author[6]), there is a passage in which Serveto describes the lesser circulation, at the same time denying the communication of the two ventricles through the septum, and assuming that the blood from the right ventricle goes to the lungs where "flavus efficitur, et a vena arteriosa (arteria pulmonaris) in arteriam venosam (venæ pulmonales) transfunditur" (it is made brighter (yellow) and is transfused from the vena arteriosa (arteria pulmonis) into the arteriam venosam (venæ pulmonales)).

In the year 1559, that is to say six years later, Realdo Colombo, of Cremona, who for fifteen years had been prosector and then successor of Vesalius in the chair of anatomy at Padua, published at Venice his work entitled, "De re anatomica, libri XV," in which, on page 177, there is a description of the lesser circulation and a confirmation of the impermeability of the cardiac septum. The author lays great stress upon this discovery and claims the priority of it: "Nam sanguis per arteriosam venam ad pulmonem fertur, ibique attenuatur; deinde cum ære una per arteriam venalem ad sinistrum cordis ventriculum defertur; quod nemo hactenus aut animadvertit, aut scriptum reliquit." (For the blood is carried through the *"arteriosam venam"* to the lungs, and there it is attenuated, thence (mixed) with air, it is carried through the "arteriam venalem" to the left ventricle of the heart; *which no one up to this time has either observed,* or left it in writing.)

It cannot be denied, that, if we consider solely the dates of the two publications the priority of the discovery belongs to Servetus, and if one could prove (as Tollin and Preyer in Germany and Willis in England have attempted to do) that Colombo had read the "Christianismi restitutio" of Servetus, then the Cremona anatomist would have to be declared guilty of plagiarism. But this is refuted by a number of incontrovertible facts, which G. Ceradini (1876-77) arranged with great acumen.

Ceradini emphasized that Valverde, a Spanish pupil of Colombo, in a text-book on anatomy published at Rome in the year 1556, *ascribed the theory of the impermeability of the septum to his teacher.* The book is preceded by an introduction dated 1554, in which the author states that he had already caused to be made numerous plates for the embellishment of his book, which must have taken at least a year. Thus *we reach the year 1553,* in which Servetus published the book which cost him his life. The assumption seems justified, therefore, that Colombo had already for some years

[5] It is absurd to believe with some interpreters of Galen that he really meant "soot." We are dealing here with one of those orthologic difficulties in that the Greek word which now means "soot" originally meant something entirely different and probably more in harmony with the opinions concerning the nature of venous blood of to-day.

[6] Henri Tollin, l. c., presents convincing reasons for believing that numerous additional copies must have been in existence during Harvey's time of Servetus' "Christianismi restitutio" and that it would be incredible to assume that such an omnivorous reader like Harvey was not familiar with the physiologic contents of this book.

taught his theory in his lectures before he published it in his text-book.

It has been demonstrated that the passage in the "Christianismi restitutio" treating of physiology was only discovered towards the end of the seventeenth century. Ceradini further calls attention to the fact that in the year 1571 G. Günther, who, as professor of anatomy at Paris, had been the teacher of Servetus and Vesalius, in describing the lesser circulation in the words of Colombo, *lauded the latter, without mentioning his own pupil Servetus,* a proof that he did not know the "Christianismi restitutio." It is also probable that it was unknown in Italy, since it was not on the "Index librorum prohibitorum" edited by the Council of Trent and published at Rome under Pius IV in the year 1564, whereas this does contain two other heretical works of Servetus, "De trinitatis erroribus."

Finally Ceradini brought forward a splendid proof of the fact that Colombo had not plagiarized Servetus, in the comparison of the two theories.

Colombo denied the permeability of the cardiac septum completely and unconditionally; he emphasized the fact that not only the vena arteriosa, but also the arteria venosa was of considerable size; he further denied—even if incorrectly—the Galenian function of breathing, that is to say the formation of "soot" in the blood and the expulsion of the same by exhalation. Servetus on the other hand denied to be sure the existence of openings in the septum, but admitted that through it "aliquid resudare possit" (something could be expelled), and upheld the Galenian theory by the assumption that the blood "in ipsa arteria venosa inspirato ære miscetur, et exspiratione a fuligine expurgatur" (in the arteria venosa itself is mixed with inspired air, and is cleansed by expiration from the "soot").

This question is a family quarrel among the Italian and Spanish anatomists and physiologists themselves, hence the sentiment due to national bias cannot be excluded in the conclusion of Luciani (professor of physiology at Rome), who says: "We will not go so far as to consider the hypothesis of Ceradini proved, that Servetus took the theory of the lesser circulation from Colombo, and tried to harmonize it with the old theory of Galen; but there can hardly be any doubt that the Cremona anatomist (Colombo) taught his theory for some time before it was published by the Spanish physician and theologian (Servetus)."

It is also of interest to determine to what extent Vesalius of Brussels was concerned in this theory, the great founder of modern anatomy, to whom Flourens (1857) ascribed the priority of the theory of the impermeability of the septum, while Henri Tollin (1884) accused him of plagiarizing Servetus, in which opinion Tigerstedt (1893) concurred.

In a recent publication[7] von Tackschath asserts that Vesalius is guilty of "plagiarism" and to have taken his anatomy—the "*Fabrica*" (1543) from Leonardo da Vincis.[8]

[7] Wien. med. Blätter, No. 46, 1902.

[8] See also Münchener med. Wochenschr., Mai 3, 1904, p. 821.

In the first edition of his great work, "De humani corporis fabrica" (1543), Vesalius says that he is forced to admire the art of the master, who through invisible pores caused the blood to penetrate from the right into the left ventricle. In the second edition of the same work, which appeared in 1555, this expression of admiration for the creator is lacking, and the author declares that he cannot understand how "per septi illius substantiam ex dextro ventriculo in sinistrum vel minimum quid sanguinis assumi possit" (he could assume any substance even any blood to pass through the septum out of the right ventricle into the left).[9]

This more correct point of view, according to Tollin, was obtained by Vesalius from the "Christianismi restitutio" which Servetus had published two years previously, in 1553. It seems likely that Vesalius was using irony or sarcasm in the above expression, for he later on admitted that "*he accommodated his statements to the dogmas of Galen.*"

But Ceradini proved convincingly, through a long series of quotations from the above work of Vesalius and also from some of his smaller publications, that Vesalius had become acquainted with the impermeability of the septum at Padua in the year 1543 through his prosector Colombo, and that he had defended it at Pisa in the year 1543, without however expressly emphasizing the necessary physiological consequence of this, that is to say the theory of the lesser circulation and the necessity, already recognized by Galen, of anastomoses between the arteria venosa and the vena arteriosa; he wished to avoid giving possible glory to Colombo, against whom he always had a grudge, because the latter had apparently sought to incite the students at Padua against him.[10]

In the "*Ergebnisse der Physiologie,*" Jahrgang II (1903), Biophysik, R. Tigerstedt presents an article on the lesser circulation (p. 533) which begins with a chapter "Zur Geschichte des kleinen Kreislaufs." Tigerstedt here accepts the opinion of M. Roth ("Andreas Vesalius Bruxelliensis, 1514-1564, Berlin") that the lesser circulation was discovered by Colombo. The doubt which is thrown upon the anatomical knowledge of Servetus in this article is by no means substantiated by the contemporary literature, nor by the impressions gained from the writings of Servetus themselves. Tigerstedt, following M. Roth, asserts that Servetus does not present real but speculative anatomy—that his main desire is to bring about an accordance between the Bible and anatomy by compilation from preëxisting books, not from actual dissections. He denies that the recognition of the impermeability of the septum was original with Servetus, but ascribes this to Vesalius, a credit, which, as can be demonstrated from Vesalius' own "Fabrica," etc., stands on very feeble evidence. For it is on this point, "the impermeability of the septum," on which every student of anatomy must re-

[9] For fuller English translation, see Sir Michael Foster, Lect. Hist. Physiol., p. 14.

[10] See Michael Foster, l. c., and Henri Tollin, Colombo's Antheil an der Entdeckung d. Blutkreislaufs. Virch. Arch., Bd. 91, 1883.

gret the uncertain language of Vesalius. Servetus, who had been prosector for Günter (Guinterius), professor of anatomy at Paris (Tollin), cannot be accused of having learnt his anatomy from books alone.

Without therefore trying to belittle the great services of Vesalius in the reformation of anatomy, one can nevertheless regard it as an established fact that he had no direct share in the discovery of the circulation of the blood. Indirectly, however, he aided in this by his refutation of numerous errors of Galen, especially the theory of the formation of blood by the liver. The fact that the lumen of the vena cava in the neighborhood of the heart is greater than at the liver, was for him a sufficient reason to return to Aristotle's theory of the formation of the blood by the heart, and to assume that not only the arteries but also the veins are offshoots from the heart.

In 1543 Vesalius was called by Cosimo I of Medici to become a professor at Pisa, where he determined to give a course in "amministrationes anatomicæ" on the errors of Galen. It is probable that among his auditors was numbered Andrea Cesalpino of Arezzo, at that time scarcely nineteen years of age, to whom belongs the fame of being the first to have recognized and demonstrated the general circulation of the blood.

In the year 1571 the physician and philosopher of Arezzo published his "Peripateticarum questionum libri quinque," in which he assumes, that in all parts of the body there is physiologically a constant transition of blood from the arteries to the veins by means of anastomoses, which he defines as "vasa in capillamenta resoluta"; the constant motion of the blood from the veins to the right side of the heart, from this to the lungs, from the lungs to the left side of the heart, and thence into the arteries he defines as "Circulatio." He was the first to recognize the arterial structure of the pulsating vessel which arises at the right ventricle, and which Galen had designated as "vena arteriosa," and the venous structure of the non-pulsating vein which was formerly designated as arteria venosa. He recognized further that the blood in the arteries is under a much higher pressure than in the veins, and that at its transition from the former to the latter the capillary anastomoses offer a greater or less resistance according to the degree of their contraction or expansion.

Twelve years after the "Quæstiones peripateticæ" appeared his books "De plantis" which alone would suffice to win for him imperishable renown as the forerunner of Linnaeus. In this work also he confirms that "sanguinem pervenas duci ad cor, et per arterias in universum corpus distribui" (that the blood is led through the veins to the heart, and is distributed by the arteries to the entire body).

In the year 1593 appeared Cesalpinus' work "Quæstionum medicarum libri II," in which he gave the experimental proofs of his theory. He observed that if in a living animal a vein is exposed and tied, and if soon thereafter an incision into the vein is made in the direction of the capillary, that the blood first appearing has a darker color, and that which flows out subsequently is lighter in appearance. From this observation he, with great acumen, deduced the physiological purpose of the anastomoses found in all organs between arteries and veins, in that he assumed: "venas cum arteriis adeo copulari osculis ut, vena secta, primum exeat sanguis venalis nigrior, deinde succedat arterialis flavior, ut plerumque contingit" (that the veins are so connected with the arterial mouths that the vein being divided, first exudes a darker venous blood, then succeeds the brighter arterial, so for the most part it happens).

A second experimental proof of the circulation he founded upon the fact that in any part of the body the tied veins swell between the ligature and the capillary origin, and not between the heart and the ligature, as ought to be the case according to Galen's conception: "intercepto enim meatu, non ultra datur progressus; tumor igitur venarum citra vinculum debuisset fieri" (for the course being blocked, no longer a flow is permitted; therefore the swelling of the veins ought to be made on this side of the ligatures) (*i. e.* between vein and capillaries)).

In spite of these brilliant experimental proofs of the theory of circulation, which Cesalpinus was the first to offer, the view was held by some, and among them the famous Haller, that he had indeed known the circulation of the blood but had only assumed it for the state of sleep, not during the awake state; they based their view upon a quite erroneous construction of a passage in which Cesalpinus assumes a certain reflux of the blood from the arteries towards the heart during the state of being awake. No one has better, and with more cogent logic, reduced *ad absurdum* the assertion of Haller than has Ceradini. It is a pity that Ch. Richet in his "Dictionnaire de Physiologie," which is now in progress, repeats the erroneous opinions of Haller concerning Cesalpinus, which had already been refuted through the historical-critical studies of Ceradini; which Ch. Richet certainly cannot have taken into account. (Luciani, l. c.)

H. Tollin, in a very thorough study of the life and work of Cesalpinus, concedes that this philosopher knew the greater circulation ("hat den grossen Kreislauf gekannt") but did not comprehend it.

A further very convincing proof of the circulation of the blood is found in the presence of the little valves, which are found in great number in the course of the veins, and which are so arranged that they only permit a centripetal flow of the blood and prevent a centrifugal flow. These valves Aquapendente knew and described, but did not comprehend their object.

This proof Cesalpinus did not take into account, with which fact Sprengel, a historian of medicine, reproaches him. It is a fact, however, that although Cannano of Ferrara as early as 1547 described a few of the valves of the vena azygos, and determined that their concave side was turned toward the heart, and although a few years later Fabricius of Aquapendente had found analogous valves in the entire venous system, and had demonstrated them to his pupils, he published his discovery "De venarum ostiolis" only in 1603, that is ten

years after the appearance of Cesalpinus' "Quæstiones peripateticæ."

On the other hand it must be stated that Fabricius, the describer of the valves in the entire venous system, did not recognize at all the function of the same, which consists in preventing the reflux of the blood in a centrifugal direction and to aid the centripetal flow during muscular activity; he thought on the contrary, that they were intended to retard the flow of the blood from the heart to the periphery of the veins. Who then was the first to base the theory of the circulation of the blood upon the function of the venous valves?

To Ceradini is due the credit of having brought to light a series of important documents which lead to the conclusion that the first to recognize the function of the venous valves was the famous theologian and canonist of the republic of Venice, Paolo Sarpi, the friend and pupil of Fabricius. It is a fact that some contemporary authors ascribed to Sarpi the discovery of the circulation of the blood. Brother Micanzio, Bartholin, Vesling, Gassendi, and Walaeus name him as the discoverer. Voss (1685) wrote that the discovery made in Italy by Cesalpinus of the circulation of the blood "Paulo Sarpi veneto in primis placuit." Vesling wrote to Bartholin that he had seen in the possession of Brother Micanzio after the death of Sarpi an autograph of the latter, *in which the circulation of the blood was described.* The famous Dutch physician Walaeus wrote in the year 1640: "Paulus Servita Venetus valvularum in venis fabricam observavit accuratius ex valvularum constitutione aliisque experimentis, sanguinis motum deduxit egregioque scripto asseruit" (observed more accurately the device of the valves in the veins from experiments on the construction of the valves he deduced the movement of the blood, and defended it in an illustrious writing (thesis)). Unfortunately, however, the manuscripts of Sarpi which were preserved in the library of the Servitians at Venice were destroyed, together with a large portion of the monastery, by a fire in September, 1769, and there was preserved only a passage cited from a letter, in Griselini's book entitled, "Del genio di fra Paolo Sarpi" (Venice, 1783), in which letter Sarpi makes allusion to that which he "had observed and written down concerning the circulation of the blood in the vessels of the animal body and the structure and function of the venous valves."

What credit then belongs to William Harvey, the British discoverer of the circulation of the blood, after Servetus and Colombo, after Cesalpinus, and Sarpi? Certainly he was not the first to correct the error of Galen relative to the permeability of the septum and to assume that all the blood passes from the right side of the heart through the pulmonary vessels into the left side: this was the discovery of Colombo and Servetus. It was not he who first recognized the presence of arterio-venous anastomoses, the passage of the blood through the same and the centripetal direction of the course of the blood in the veins: this was the great discovery of Cesalpinus. It was not he, who first described the venous valves, for already Cannano knew of them and his teacher Fabricius d'Acquapendente described them in detail—it was not he who discovered the physiological importance of the same for the circulation; this was probably the discovery of Paolo Sarpi. And yet great credit is due to Harvey, for the reason that he more clearly defined the theories of his predecessors, and firmly established them by numerous vivisections and ingenious experiments. The modern Italian physiologists (Luciani,[11] l. c.) accuse him of having committed a great wrong by trying to claim the glory of the discovery, not mentioning the names of Cesalpinus and Servetus, and making it appear that he did not know of their works.

After the historical-critical studies of Ceradini and also those of Tollin (which agree in this point) it would be absurd to assume that Harvey was not fully acquainted with the works of Cesalpinus, which appeared at Venice in the year 1593, that is, five years before Harvey took up his abode at Padua, where he remained four years (1598-1602) as the pupil of Fabricius d'Acquapendente. If he remained silent in the face of the charges of his contemporaries Micanzio, Vesling, Walaeus, Riolan, Bartholin, and others, who accused him of plagiarism, it was evidently because he wisely wished to refrain from entering into a discussion in which he had much to lose and nothing to gain.

In spite of all this his pamphlet of 72 pages, which appeared at Frankfurt in the year 1628, "Exercitatio anatomica de motu cordis et sanguinis in animalibus" is without doubt the masterpiece of a man of genius.

Even at the present day, after the lapse of more than two and one-half centuries of scientific investigation, this "oposculum aureum," as Haller called it, calls forth admiration of the reader, by the clearness of his ideas, and the logical arrangement of the observations, all of which were based on vivisection. With the exception of a few inaccuracies and errors, everything in the book is well observed and well conceived, and it can still at the present day serve as an introduction into a more detailed study of this interesting subject.

Upon laying bare the cardiac region of living animals, he observed that the heart is alternately in motion and at rest. During systole it rises, and with its apex moves the parietes of the chest; it contracts in its entirety, and especially in its lateral portions; it becomes hard, like the muscles of the arm when they contract, and in the case of the cold-blooded animals it grows pale, because all the blood is sent out from its cavity. Pulse of the arteries is synchronous with systole of the heart. When the heart is at rest, the arteries also cease pulsating. If one open an artery, the blood gushes forth violently at each systole. Accordingly, at the moment of systole the blood is driven into the arteries, and cannot flow back, because the cardiac valves prevent reflux.

Like the ventricles, so also the auricles contract and relax, but earlier than the ventricles. The motion seems to start from the atria, proceeding thence to the ventricles. When the

[11] See Luigi Luciani, Physiologia, Vol. I, p. 125, translated into German from the Italian by Silvestro Baglioni, Winterstein, 1904.

heart dies, the left ventricle is the first to stop, then follows the left auricle, then the right ventricle, and the "ultimum moriens" as already Galen had observed, is the right auricle. If one cut through the apex of the heart at a moment when only the right auricle continues to contract, one sees blood coming forth at each contraction. Therefore the blood is driven into the ventricles by the contraction of the auricles, and not through the suction produced by the expansion of the ventricles.

The function of the motion of the heart is to force the blood coming from the veins into the arteries and thus distribute it over the entire body. Since the interventricular septum is impermeable, all of the blood, as has been recognized by Colombo, must go by way of the vena arteriosa and the arteria venosa through the lungs in order to pass from the right into the left ventricle. In all of this there is nothing essentially new, only the correction of some errors of Galen relative to the motion of the heart.

The conception of the general circulation is clearly expressed by Harvey in the following words: "... patet sanguinem in quodcumque membrum per arterias ingredi, et per venas remeare; et arterias vasa esse deferentia sanguinem a corde, et venas vasa et vias esse regrediendi sanguinis ad cor ipsum; et in membris et extremitatibus sanguinem (vel per anostomosin immediatem vel mediate per carnis porositates, vel utroque modo) transire ab arteriis in venas; sicut ante in corde et thorace a venis in arterias: unde in circuitum moveri, illinc huc et hinc illuc, e centro in extrema scilicet, et ab extremis rursus ad centrum, menifestum fit" (it is evident, that the blood enters every portion of the body through the arteries, and returns through the veins; and that the arteries are the vessels carrying the blood *from* the heart and the veins are the vessels and ways of returning the blood TO the heart again; and that in the members and extremities the blood passes from the arterics into the veins (either by *immediate anastomosis,* or mediately through *porosities* of the flesh, or by some other way?); as before was made manifest, in the heart and thorax from the veins into the arteries; thence to move in a circuit, now in one direction, now in the reverse, manifestly from the center to the extremities, and from the extremities back to the center.) From his own words we recognize that Harvey evidently was ignorant of the capillaries.

To prove his assertions, he furnished experimental proof of the three following theses:

1. The blood propelled by the contraction of the heart passes incessantly from the vena cava into the arteries, in such quantities, "ut ab assumptis suppeditari non possit, et adeo ut tota massa brevi tempore illinc pertranseat" (that it could not be furnished by the food consumed, and in a measure that the entire mass will flow through thence in a brief time).

2. The blood propelled by the pulsations of the arteries penetrates incessantly into every member or every part of the body, "majori copia multo, quam nutritioni necessarium sit, vel tota massa suppeditari possit" (in far greater abundance than is necessary for nutrition, even if the whole mass (of the body) could be supplied).

3. Ab uno quoque membro ipsas venas hunc sanguinem perpetuo retroducere ad cordis locum" (from any member its veins perpetually carry back the blood to the heart).

The demonstration of the first thesis is the most substantial portion of Harvey's work. Starting with the capacity of the right ventricle in human corpses (which is slightly more than three ounces of blood), he emphasizes the fact that a considerable quantity of blood must be driven into the arteries at each systole, in consequence of the size of the orifices (?) and the force of the contraction. However large this quantity be, it must be in proportion to the difference between the capacity of the contracted and the dilated ventricle. If the heart of man or of other animals convey only a single dram of blood at each contraction, and if in half an hour it perform a thousand contractions, the result is, that the heart in this short space has driven ten pounds and five ounces of blood into the arteries, a quantity which is much too large to be supplied by the food taken into the body, unless the blood return in the same way. One need not open the aorta, but merely any small artery, in order to cause all the blood of the body to gush forth in less than half an hour, as Galen already observed.

The demonstration of the second thesis is only an expansion of the experiments and ideas of Cesalpinus. If one apply a tight ligature to an arm, as in the case of amputations, pulsation of the arteries ceases in the periphery, while the arteries toward the center beat more violently and swell. The hand and arm cool after some time. If the ligature be only loose, as in the case of blood-letting, then the arm swells below the ligature, and the expanded veins appear prominently. Above the ligature on the contrary they become invisible. By the tight ligature the passage of the blood through the arteries is prevented, while the loose ligature prevents the course of the blood in the veins. Therefore the blood passes from the arteries into the veins. Here Harvey, with only slight changes, repeats the final deduction of Cesalpinus: "... apparet qua de causa in phlebotomia ... supra sectionem ligamus, non infra" ("from which cause it is manifest that in phlebotomy we bandage above the cut and not below").

Also the conclusion drawn from this, that the blood flows toward the various organs in much larger quantities, "quam nutritioni sufficiens sit" ("than is sufficient for nutrition"), is taken from Cesalpinus, who designated as "alimentum nutritivum" that which the blood carries along for the nourishment of the organs, and as "alimentum auctivum" (growing) the part which returns to the right side of the heart, after passing from the arteries through the capillaries into the veins.

The proof of the third thesis is founded entirely upon the physiological function of the venous valves. Harvey treats this point with great acuteness, since it is best adapted to convince the incredulous, and he adds four illustrations of ligatured arms (one of them being simply a reproduction of "*Figura I, Tabulæ II, brachii vivi ad sanguinis missionem*

ligati" (living arms ligated to hinder the flow of the blood) from the treatise of his teacher Fabrizio (Fabricius ab Aquapendente), *"De venarum ostiolis,"* which exhibit the veins swelled varicosely at the place of the valves. The venous valves do not serve the purpose of preventing a superfluity of blood in the lower portions of the body, for they occur also in the venæ jugulares, which go from above down, similarly in the venæ emulgentes, mesentericæ, etc. They serve rather to prevent a rushing of the blood from the larger into the smaller veins, so that the latter may not tear and become varicose, they prove that the blood in the veins does not flow from the center to the extremities, but from the latter to the center. Injections through the larger into the smaller veins are often arrested by the resistance of the valves, while in the case of injections through the small into the large veins there is no obstacle.

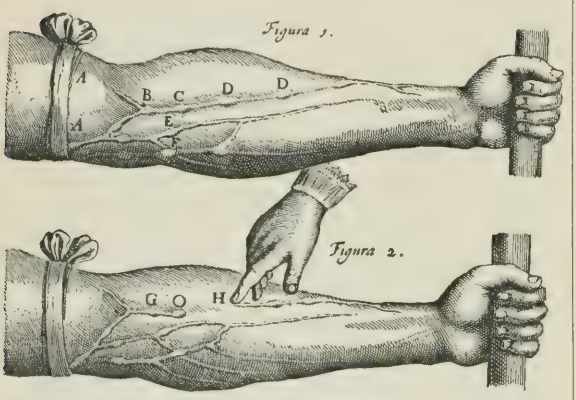


Fig. 1 is a reproduction (Photozinkography) of the two first figures of Harvey's work, edition 1639, ex officizna Joannis Maire, Lugduni Batavorum.

Fig. 1 is an exact imitation of the illustration in Fabrizio's writing "De venarum ostiolis." At *AA* the arm is ligated as is customary in venesection. One sees the swollen veins, which show enlargements at the points *B, C, D, E, F,* which proceed from the valves. These are not only found at the bifurcations (*E, F*), but also at (*C, D*).

Fig. 2 shows the same arm in which the blood has been forced from *O* to *H*, by drawing the finger forcibly along it from *H* to *O*. The portion of vein *H* to *O* appears to be obliterated, because a valve exists at *O*, which prevents the blood from flowing back to *H*, and the finger pressing upon the vein at *H* prevents the blood from flowing in from the peripheral veins.

If on the ligatured arm one press the blood out of a vein with the finger, one sees that when the blood arrives above a nodule (which shows the position of a valve) (nodule) it cannot flow back again, and the portion of the vein between the nodule and the finger appears obliterated.[12] Accordingly the function of the venous valves is the same as that of the semilunar valves of the aorta and the vena arteriosa (arteria pulmonaris), which close the orifice and prevent a reflux of the blood.

One would think that the theory of the circulation of the blood, which had already been demonstrated by Cesalpinus, would, through its perfection at the hands of Harvey, have immediately been accorded scientific citizenship, and be recognized by all. But opponents were not lacking, and among the most important and at the same time most persistent of them was Jean Riolan (Riolanus), a famous Parisian anatomist, and Kaspar Hoffmann, a leader of German science of that period, who had been, like Harvey, a pupil of Fabricius d'Aquapendente at Padua. They recognized, indeed, that the new doctrine would result in the total collapse of the system of medicine of the period, and every means seemed justified in preventing this, which in their eyes at least seemed a deep disgrace. It is scarcely necessary to say that this opposition (although it disclosed some mistakes and errors of Harvey's work) only aided in propagating and advancing the new theory. And thus the remark of Ceradini seems very apt, that "Harvey owed his success to the opposition of the Parisian anatomist, who, upon Fabricius' death was considered the greatest authority in Europe; and the error of the partisans of the Englishman arises from the parallel which they drew from the impression which his writings made in the scientific world, as compared with those of Cesalpinus. . . . Had Cesalpinus during his life met with a Riolan, to accuse him of plagiarism, absurdity, and of heresy, the very slow development of his ideas concerning the circulation, in lectures covering a period of more than thirty years (first at Pisa then at Rome), would have been impossible without discovering the possible results and appplications of the same, no one could have taken from him the great renown of his discovery."[13] Furthermore, Harvey himself was at the beginning so far from having any idea of the far-reaching consequences of the doctrine of the circulation of the blood, which he had learned from Andrea Cesalpinus, that he only thought of printing it after he had for nine years treated of it in his lectures; he was only impelled to do so by the fact that this doctrine had made both friends and enemies for him, and that the latter made a great stir about it. And even after the appearance of his book, in the year 1649, the physiological importance of the theory seemed to him so problematical, that in his answer to Riolan, who declined to accept the theory, because he could see "neque efficientem, neque finalem causam" (neither the influence, nor the final effect) he had no better reply to make than to say: "Prius in confesso esse debet quod sit, antequam propter quid inquirendum. . . . Quot sunt in physiologia pathologia et therapeia recepta, quorum causas non novimus, esse tamen nullus dubitat?" (first it ought to be conceded what may exist, before inquiring what it means or wherefor. . . . How

[12] See Figs. 1 and 2, above.

[13] Ceradini here means that the complete comprehension of a discovery is often not made by the discoverer himself, but he may be brought to a wider comprehension of his contributions to science by the opposition of men of authority.

many things there are received in physiology, pathology and therapeutics, whose causes we know not, yet no one doubts their existence?)

As long as the theory of Aristotle flourished, which had been rehabilitated by Cesalpinus and Harvey, that the function of the lungs consisted in refreshing the blood, and that this organ, in which the blood was again made spirituous and thin was nourished by the thick blood flowing back from all the organs; as long as especially the place of blood-formation remained unknown, and also the channels through which the products of digestion reached the circulatory system; just so long did the theory of the circulation of the blood remain without its true significance, and it could only be regarded as a physiological curiosity.

To judge from certain passages in Galen, it seems as if Herophilus and Erasistratus, the heads of the Alexandrian school (300 B. C) had seen the chyliferous vessels in the mesentery of the sheep. Towards the end of the 18th century Portal remarked, as in fact also Fracassatus had done more than a century earlier, that the celebrated Roman anatomist Eustachius,[14] in studying the course of the vena azygos in the horse, had observed the thoracic duct and even some of the valves of the same. But it is certain that every trace of these accidental and isolated observations had vanished to a vague tradition, when Gaspare Aselli of Cremona, professor of anatomy at Pavia, found, in 1622, the chyliferous vessels in the mesentery of the dog, designating them by the name of lactiferous vessels. So happy was he at having found what he had been seeking, that, as he relates, "conversus ad eos qui aderant: εὕρηκά, inquam cum Archimede" ("I turned to those who were present: I exclaim with Archimedes, Eureka"). But as yet he had no idea of the true function and physiological importance of these vessels.

In the year 1648 Pecqet, a young physician of Dieppe, who was studying in Montpellier, found that the lactiferous vessels do not send their contents to the liver, as Aselli had believed, but to a large vessel, the thoracic duct (re-discovered by him after Eustachius) which empties into the subclavian vein. Two years later Rudbeck, a Swede, discovered the lymphatic vessels of the liver, and recognized that they also send their contents to the thoracic duct. Finally, in the year 1652, the famous Danish anatomist, Thomas Bartholin, discovered the same vessels in all parts of the body, and found that all of them, together with the chyliferous vessels, flow into the thoracic duct. In order to give further scope to the theory of the circulation of the blood, ascribed by him to Harvey, he published a new edition of his anatomy "*ad sanguinis circulationem reformata,*" being correctly convinced that he had furnished a new argument in favor of it, indirect to be sure, but nevertheless valuable.

According to Ceradini, "Riolan himself, the upholder of every old doctrine, and the opponent of everything new, in this case withheld the sharp arrows of his criticism, in order not to see them rebound harmlessly from the strength of facts. Harvey, however, DENIED THE EXISTENCE OF THE CHYLIFEROUS and LYMPHATIC VESSELS, and EVEN THE FUNCTION OF THE THORACIC DUCT, *and died without being converted, in the year 1658,* six years after the death of Bartholin. Luciani (professor of physiology in Rome), in his elaborate handbook on human physiology, expresses surprise and regret that Sprengel, the famous historian of medicine, scarcely mentions this "*ugly trait in the character of the Englishman, this contempt for every discovery which was not his own, a blemish which would be inexcusable, even if Cesalpinus had not demonstrated the circulation of the blood before him.*"

In order to complete the new theory, and to bring it to a state of absolute certainty, there was now only lacking the last decisive step, the discovery of the capillaries of the blood and the direct observation of the circulation of the blood through these capillaries from the arteries to the veins. "Supererat" (it remains), as Haller said, "ut ipsis oculis circuitus sanguinis subjiceretur" (that the circulation of the blood be subjected to the eyes (be actually seen)).

Galen, who, as already mentioned, was the first to assume direct communication of arterial and venous vessels in the organs, thought of a kind of direct anastomoses or a simple meeting of the two kinds of vessels. This was not in accord with the idea which Cesalpinus had formed; the latter conceived that the junction was made "per vasa non desinentia, ulterius transmeantia" (by vessels not stopping, but passing through), or "per vasa in capillamenta resoluta" (by vessels broken up into hairs (threads)) (which Harvey changed to "per carnis porositates") (through porosities of the flesh), and Cesalpinus thus guessed the existence of a new kind of vessels, which unite the arteries with the veins and which then were called capillaries.

Marcello Malpighi, with the aid of the microscope, was the first to observe the motion of the blood in the capillaries of the lungs of the frog. This was in 1661. With just pride he exclaimed: "Talia mihi videre contigit, ut non immerito illud Homeri usurpare possim ad rem præsentem melius; magnum certum opus oculis video" (it has happened to me to see such things, that not undeserving I might in the present instance use the saying of Homer: I see with my eyes a sure great work).[15]

After Malpighi, vain attempts were made by Leeuwenhoek, Cooper, and Haller to extend these observations also to the warm-blooded animals. The first to succeed in this was Lazzaro Spallanzani, who hit upon the idea of making use of the hen's egg during the process of development of the chick. The enthusiastic words with which the great physiologist reports his discovery cannot but provoke a smile. "For a long time I had been burning with the desire to discover the circulation of the blood also in the case of the warm-blooded animals, to observe it in the same degree in which I had noticed it in cold-blooded animals, and thus these vessels (the vasa umbilica of the chick) attracted my attention more than

[14] Opuscula anatomica, Venetiis, 1564.

[15] Cf. Fig. 48.

anything else, because they belonged to that species of animal. Since the room in which I was, did not have sufficient light and I was determined in some way to satisfy my curiosity, I resolved to examine the egg in the open air, by direct sunlight. After I had fastened it to the small Lyonet apparatus (a small microscope, used by Spallanzani) I immediately focused the lens upon it, and in spite of the flood of light which surrounded me, I could, by partly closing my eyes, distinctly see the blood circulate through the entire complex of the arterial and venous umbilical vessels. Overcome by this unexpected pleasure, I felt at liberty also now to cry out: 'I have found it, I have found it!' I made the discovery in May, 1771, and in the summer vacation of that year I took pains to develop it suitably."

These observations of Malpighi and Spallanzani, separated by a century, constitute two of the chief events in the history of medicine. The glory of the first direct observation of the circulation of the blood belongs undoubtedly to the Italian physicians. Modern scientists, with more perfect microscopes and more advanced technical skill, have only been able to perfect the description of the circulation of the blood as seen under the microscope.

In speaking of Servetus, Sir Michael Foster does not concede to him any marked influence on the development of anatomic thought of his day, and declines to regard him as a real link in the chain which leads from Galen to Harvey.[16] He would concede to the writings of Servetus only isolated bits of truth, floating along the stream of human thought, by the side of other truths, the outcome of the labors of other men. But though Sir Michael Foster speaks in the diminutive concerning the work of Servetus, he makes use of this very author's work to minimize the merit of another contributor to the history of the circulation, namely, Matheo Realdo Colombo; for he suggests that Colombo might have taken the idea of pulmonary circulation from Servetus, and his reason is that in 1546 Servetus sent to Curio in Padua a manuscript copy of his "Restitutio." "This Columbus may have seen. Again, when the edition of the published 'Restitutio' was burnt in 1553, some few copies escaped. One of these may have found its way to Rome before Columbus had sent his work to the press." Tollin[17] and Preyer[18] have arranged the quotations from Colombo and Servetus concerning the lesser circulation side by side, suggesting that Columbus learned what he knew from Servetus.

Sir Michael Foster furthermore attempts to support his charge of the plagiarism of Columbus from Servetus by what he calls an "unabashed attempt to assert ownership of the discovery of the third ossicle of the ear, the stapes." According to Fallopius, the stapes was first described by Ingrassius of Palermo, a Sicilian, in 1548. This may be, as Foster states, a theft, but it is not absolutely proven, because at the present day, two physiologists or anatomists, in different countries, have been known to make and claim an identical discovery simultaneously.

The character of Colombo is represented as having been that of a "vain and ungrateful successor of Vesalius,"[19] and his standing, it is indicated, suffered by his fulsome adulation of Pope Pius IV, a pope whose character has met with much criticism.

From the standpoint of critical conservatism we cannot conceive that the charges of plagiarism and theft against Colombo have been satisfactorily proven. At least they would not be accepted as proven by a judicial mind. I have already given the proofs in the preceding on the authority of G. Ceradini,[20] which are incontrovertible facts, that Colombo could not possibly have plagiarized Servetus. His accurate descriptions of the pulmonary circulation may be the results of his own research and subjective analysis. Some doubt is thrown on Ceradini's conclusion by the incomparably precise historic researches by H. Tollin,[21] who does not consider that Colombo is original, but simply has confirmed what Servetus described before him.

Concerning the merits of Andreas Cesalpinus,[22] Foster[23] suggests that "they were not the outcome of patient research, or real study of the phenomena themselves, but may have been flung out in the spirit of controversy, as effective assaults upon the accepted doctrine of the times." In the preceding, however, I have given the evidence that we have no right to question, that the theories as announced by Cesalpinus were not the outcome of real study of the phenomena themselves.

A personal and systematic study of Cesalpinus' works undeniably gives the impression that he was a man of most vacillating character, of insufficient force of conviction even where there was every probability that his views were correct. But even his greatest opponent, Tauriel (of Montbéliard), has much to say in praise of his versatility and the inventive power as displayed in the "Quæstiones peripateticæ," and that these talents when coupled with "love of truth and piety" would justify us in expecting great and useful things of Cesalpinus." ("Qua sua singulari facilitate poterat prodesse plurimum—res magnas et humanæ societati utilisimas præstare possunt.")

It cannot lead to a just opinion of Cesalpinus, to merely glean here and there in his works; isolated patches of his writings must inevitably present a disconnected, illogical character, whereas in truth his argument is as homogeneous and consequential as that of Colombo—whom Harvey honors and quotes to the total exclusion of Cesalpinus.

It is very regrettable that the great Haller made an erroneous construction of a passage from Cesalpinus, in which a reversal of the present idea of the circulation was assumed to take place during the waking state (a certain amount of reflux

[16] Lectures on the History of Physiology, p. 24.
[17] Virchow's Archiv., Bd. 91, 1883.
[18] Samml. physiolog. Abhdl., 1876.
[19] Puschmann Handb. d. Geschichte d. Medicin, Bd. 11, p. 331.
[20] Loc. cit.
[21] Loc. cit.
[22] See preceding.
[23] Loc. cit., p. 35.

of blood from the arteries to the heart during the waking state).[24] The forcible logic of Tollin[25] and of Ceradini have set the views of Cesalpinus in the right light; and proven that he was a physiologic experimenter of ability. He had not only grasped clearly the pulmonary circulation, but also the systemic circulation. There is no doubt whatever that he knew that the flow of blood to the tissues took place by the arteries, and that the return of the blood from the tissues took place by the veins and not by the arteries. The published works of Colombo and Servetus to my mind represent independent and individual conceptions. The charges of plagiarism of one from the other, are ingenious speculations.

It cannot possibly deduct from the brilliancy of Harvey's genius to have the work of his predecessors set in the right light. His admirable combination of anatomical features with physiologic function, his conception of experiments, both original and conclusive, testing the validity of his explanations, all combine to complete the picture of a physiologic thinker of colossal ingenuity. If other workers preceding Harvey fell short of his results, it may of course have been due to a lesser intellectual endowment, but it may also have been due to the fact that they were working in countries in which scientific research was under the ban of Church and State. Furthermore, path-hewing is more difficult than path-widening. The older and preceding workers in any department of science do not, as a rule, grasp the entire truth concerning the relation of things. Scientific exploration takes place, as a rule, bit by bit, sometimes by strenuous and painful endeavor. The mental or subjective conceptions preceding the experiment being often more laborious than the actual devising of experiments to test the validity of the conception. All this in the discovery of the circulation of the blood took centuries.

As grateful recipients of the labors of the historic apostles of physiology, it behooves us to maintain a judicial mental attitude and interpret the contributions of each physiologic worker from the aspect of the condition and influences—political, religious, scientific, and otherwise,—that were predominating at his time, and in that light it is astounding to observe how near to the truth Servetus, Matheo Colombo, and Cesalpinus came with their crude methods of subjective and objective analysis, and we will have to sum up in one abstract sentence with Professor L. Landois that "William Harvey, a pupil of Fabricius (until 1604) finally constructed, between the years 1616 and 1619, partly from his own investigations and partly from the results of former observers already mentioned, the picture of the circulation of the blood, the greatest physiologic achievement, which was published in 1628 and marks a new epoch in physiology."

A Résumé of What We Have Learned from the Literature Quoted in the Preceding about Harvey and His Relation to His Predecessors.

We gather from Harvey's own writings and the scholarly studies of Henri Tollin,[26] that, seven years before his death, Harvey plainly teaches that before him there was a knowledge of the circulation of the blood. In "De Motu Cordis" and in his writings to Riolan he teaches that Realdo Colombo has shown that the blood does not pass from one ventricle into the other through the middle wall of the heart, but through a long circuit through the lungs. Harvey imparts to his friend Boyle that he got his first suggestion of a circulation of the blood from his Paduan teacher, Hieronymus Fabricius ab Aquapendente, led to the idea by meditation over the function of the valves in veins, and to his friend Ent, that Fra Paolo Sarpi (1623) had left a writing on the uninterrupted return of the blood (to the heart) five years before Harvey published his. Harvey declares it the duty of the scientific anatomist to learn the experiences of his predecessors, to prove and to use them. He abundantly makes use of this right and therefore walks in the foot-prints of Galen and Hippocrates, of Pliny and Aristotle, of Fernel and Vesalius, of Colombo and Aldrovandus, and of many, many other authorities. Harvey regards the moving blood as inseparable from the spirit, which first gives it movement, warmth, feeling, power of nutrition, even something heavenly, corresponding to "the element of the stars." Harvey makes this probable to us by many relative thoughts, which he has drawn from not only Realdo Colombo, whom he cites several times, but also from Michael Servetus, Sarpi, and Andreas Cesalpinus. But through the proud, independent, indomitable peculiarity of his character, Harvey makes plain to us why, where the renown of a discoverer was at stake, he could not bring himself to say: "I am not the discoverer, but yonder Aristotle and Aquapendente, there Aselli, Pequet, Rudbeck, and Bartholin, there again Caspar Hoffmann, here finally Sarpi, Cesalpinus, Colombo, and already before them Michael Servetus."

I am well aware that Tollin's[27] conclusion may vary from the current, traditional jubilation over the great Harvey, the demonstrator of the entire circulation of the blood. But Tollin, if abused for this variation, will answer with the words of his teacher, William Harvey: "Trust in your own experiences, not in those of others" (propria experientia nitendum est, non aliena (Opp. 172)).

The completion of the discovery of the circulation of the blood by Malpighi and Leeuwenhoeck, by Eustachius, Aselli, Pequet, Rudbeck, and Bartholin, by the injections of Swammerdam, Horne, and Ruysch, the observation of invertebrate animals on the part of Willis and Milne-Edwards, by the discovery of graphic methods, by the observations of the vasomotor nerves on the part of Bernard, Brown-Séquard, Ludwig, lead Chapman[28] to the conclusion that "*the* SPIRITUAL DEVELOPMENT *of humanity is also a growth that is governed by life-laws, and that a discovery, although if it was not made by him to whose name it is wont to be attached, yet at the appointed time would have seen the light of the world.*" All circum-

[24] See preceding.
[25] Loc. cit.
[26] Loc. cit.
[27] Henri Tollin, Arch. f. Pathol. Anat., Bd. XXXI, 81, Heft I.
[28] Loc. cit.

stances show that towards the end of the sixteenth century intellectual Europe was ripe for the acceptance of the discovery of the circulation of the blood. If it had come a few centuries sooner, it would have died at its birth. Italy and particularly Padua were alive with speculations, hypotheses, and theories concerning the course of the blood through the body. One who will compare the Latin original of Harvey's writing upon the circulation with the writings of the great Italian anatomists and physiologists of the sixteenth century, will be astonished at the similarity of thought and expression. (The same mode of thought and expression pervade both.)[29] In the method of his investigation, observation, and conclusions, Harvey is essentially Italian. An Englishman by birth, an Italian in thought, Harvey lived and died as a student of Padua. Thus Chapman returns to where he started out. Between Galen and Servetus, the second and third epochs of the discovery, Chapman establishes an interval of 1718 years; between Servetus and Cesalpinus 40 years; between Cesalpinus and Harvey 35 years. When Servetus stood forth, he risked that his discovery might be burned with himself. When Harvey stood forth, all had been prepared. He came, considered, and gained the victory.

Tollin pointed out what an advance in the investigation of the history of the discovery of the circulation of the blood, even in Harvey's fatherland, since 1878 (the 300th anniversary of Harvey's birth), we have to record. Before 1878 it was not only the dogma of the profane crowd of the educated but also of the professionally educated in England, that as Minerva from the head of Jupiter, even so fully and entire, the discovery of the circulation of the blood sprang from the head of Harvey. Now even in England it is said: When Harvey came, everything was fully ripe. If he had not harvested, then at that time another would have come and gathered in the harvest. The seed sowing was the work of the Spaniards, especially of Michael Servetus; the watering, the care, the pruning the work of the Italians, especially of Colombo, Cesalpinus, Fabricius de Aquapendente. To Harvey remained the honorable, remunerative, although always troublesome work of the harvest. But what we possess to-day, we possess through him who harvested it for us. And for this Tollin designates the gifted Harvey, "the great Briton, the pattern of all harvesters and classifiers."

William Harvey, armed only with a magnifying glass, accomplished such great things that one cannot express what this genius would have accomplished had he, like Malpighi, been furnished with a microscope. But the discoverer of the blood circulation is not Harvey, however much, misled by the favor of two kings and the almost idolatrous reverence of his nation, he sought to convince himself that he was such. And he did convince himself and finally did believe in it, because this belief only too soon had become the dogma of his nation. But, in the moments when he is candid, he acknowledges that several persons before him, induced by Galen's authority and that of Colombo and Servetus, beside other reasons, had taught the truth about the blood-vessels and had expressed the opinion which he now claimed as his own; yes, that many, long before him, had known of a blood circulation, by means of which continually the blood passed from the arteries into the veins and from the veins returned to the heart; that he himself had gladly and diligently read the books of those who had borne the torch of truth before us, that he willingly paid due respect to those old authorities and only *had not mentioned particularly all of the modern ones in order not to give occasion for disputes;* and that it was he who had erected upon firm and necessary foundations, more distinctly, more orderly, and fully corresponding to the actuality, the blood circulation discovered before him.

We once more affirm Harvey, the author of "De motu cordis et sanguinis," 1628, did not discover the lesser circulation. This Servetus discovered in 1546. Harvey did not discover the greater circulation. This Cesalpinus discovered in 1569. Harvey did not discover the venal valves. These Jacob Silvius, Sarpi, and most accurately Aquapendente discovered in 1574. Harvey did not furnish the clear-sighted proofs of the circulation. These were given by Servetus, Colombo, Valverde, Aranzi, Ruini, Rudio, Sarpi, Cesalpinus, and Aquapendente. Harvey never saw the circulation of the blood. Malpighi saw it several years after Harvey's death (1661).

Strictly speaking, Harvey did not even describe the circulation, but a double half circulation. Whether in the lungs and in the extremities the arterial endings were in communication with the commencement of the veins by anastomosis, or by infiltration of blood into the pores of the tissues, he never dared to decide, because the magnifying glass here failed to tell him. And so, since two half circulations suddenly end without a demonstrable continuation, there is no actual, no completed circulation.

Nevertheless, even then Harvey still remains an incomparable genius. For "*by the accuracy and thoroughness of his deductions, by the skillfulness, by the industry and the abundance of his experiments, by the carefulness and the delicacy of his observations, by the keenness and shrewdness of the proofs, by the clearness and truth of the conclusions drawn, by the novelty and importance of the interposed reflexions, above all by the harmonious connection of the whole,*" William Harvey, the great regius predemonstrator of the blood circulation, the movements of the heart and of the blood, has lifted these from a hypothesis of the darkest possibility to the clearest probability, from the recesses of single obscure studies to the shield of public opinion, from the individual views of a few favored ones to a dogma everywhere sanctioned. And in this sense one can indeed say with Tollin: "Without the school of Padua, yes without Erasistratus, Aristotle, Galen, Servetus, Vesalius, Colombo, Cesalpinus, Aquapendente, we would have had no Harvey, but without Harvey no discovery of the blood circulation."

Harvey quotes among the authorities known at and previous to his time Aristotle, Galen, Erasistratus, Vesalius, Realdo

[29] Tollin: Loc. cit.

Colombo, and Fabricius de Aquapendente. He does not cite Michael Servetus nor Cesalpinus, and yet he must have been acquainted with their works, for his methods of thinking show many resemblances to that of these writers. It is absurd to assume that such an omniverous reader as Harvey, who studied four years at Padua, where the works of these two men were widely known, was not acquainted with their writings. The omniverous reader, Harvey, who is described as accompanying King Charles I, and taking care of the princes, and during the battle of Edgehill (Oct. 23, 1642), as sitting at the outskirts of the fight under the hedge reading a book (Aubrey).[30] Furthermore, Robert Willis,[31] the greatest Harvey connoisseur in England, actually asserts that Harvey was a free-thinker like Servetus and Cesalpinus, and even an Antitrinitarian, so that he must have been in religious sympathy with these two men, and for this reason again he probably sought and was familiar with their works. And yet we will have to excuse him for not quoting these two early discoverers for the following reason:

Because of his heretic work "De Trinitatis Erroribus," Michael Servetus was burned at the stake at Geneva, in 1553.

Cesalpinus, free-thinker like Servetus, friend of Trismegistus and precursor of Spinoza, could only save his life by retracting.

Matteo Realdo Colombo was a diplomat, clerically inclined, friend of several cardinals and flatterer of the inquisitorially-minded pope Paul IV, his memory was held in high esteem at the English Court, whose queen was a devout Catholic, and whose king was secretly her ally. A hater of the Protestants, an enemy of all Puritans, and still more of the free-thinkers, a systematic adherent of a strict bishopric régime, the royal patron of Harvey was the man who sent the members of Parliament into prison, who made the method of punishment severe to the utmost to Anabaptists and Antitrinitarians, and applauded the massacre caused by Ireland's Catholics among the Protestants. As is well known, the king was beheaded in 1649.[32]

The Protestant England, with its independent spirit of inquiry, to whose free manner the Harvey jubilants attributed Harvey's great discoveries, did not exist at his time, and not for a long time after it. Harvey died the 3d of June, 1658. And still King Charles II, son of the executed Charles the first, forced on Bartholomew's Day, by his Acts of Uniformity, two thousand English clergymen to resign their positions because they refused to subscribe to the thirty-nine articles of the King's faith. Even quiet prayer-meetings in the attics were considered treasonable. The heretics were banished. None of the exiles were allowed ever to come again within five English miles of their villages or any English cities.

Twelve years after Harvey's death the nonconformist act was rendered still more severe. Indeed twenty years after his death nobody could venture to adhere publicly to Cesalpinus and Michael Servetus. Up to 1828 the Acts of Uniformity of Charles II governed, which excluded all nonconformists from Parliament and civil service, also from the office of a royal court physician, which meant so much for Harvey. Under the son of Harvey's patron, 80,000 Englishmen had to suffer all kinds of persecution because they refused to take oath to the faith of the State. Eight thousand alone had to go to prison for their faith.

James II, successor of Charles II, declared himself openly a Catholic, to destroy the last remains of the free faith by strict government without Parliament.

But his son-in-law, William of Orange, thirty years after Harvey's death, set up the famous Acts of Toleration in 1689. But free-thinkers, like Peter Bayle, were dismissed from their offices (1693) and those who sided with Servetus, called the Socinians, were expressly excluded from every public tolerance.

There are some who lauded Harvey's character up to the skies, just as they called (according to the legend) Harvey's mother the best of all women, probably because one knows nothing of her. But has nobody discovered a predestination as a martyr in a man who always kept his faith as secret as possible, and who deserted his royal benefactor as soon as the luck left the king's banners. No wonder, therefore, that Harvey does not mention Cesalpinus and Michael Servetus, even had he known them by heart.

The fruit of an intellectual deed is frequently more evidenced in the incentive which that deed gives to investigation than in the actual contribution to science made therein. An immense industry was developed by the exact proofs of the circulation furnished by Harvey, diseases were conceived of in a new light, efforts at transfusion were made, and of injection of remedies into the circulation.

The discovery of the circulation of the blood was the work of almost a millennium from Aristotle and Galen to Harvey, but the one who first logically drew true consequences out of hundreds of years of preceding work, and upon whose broad intellectual shoulders all subsequent investigations rested, was William Harvey; and to-day, 328 years after his birth, we may side without reservation with the words of Bartholin: "At Harveyo omnes applaudunt circulationis auctori!"

[30] Foster: Loc. cit., p. 42.

[31] Loc. cit.

[32] A court physician, under such a tyrannical prince, who would have dared to confess himself to Cesalpinus or even to Michael Servetus, would have certainly been executed, like Harvey's contemporary, the Saxon Chancellor Nicholaus Crell, who was beheaded for heresy at Dresden, the 23d of October, 1591, after ten years of imprisonment in a fortress. And Crell was not even a free-thinker, but a Protestant, who had the courage to prefer to be called a Christian, instead of a Lutheran or a Calvinist.

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COMPARATIVE SURGERY:

WITH ILLUSTRATIVE CASES,

By C. M. Faris. H. C. Thacher, J. F. Ortschild, and F. C. Beall.

AND AN INTRODUCTION,

By Harvey Cushing.

It is the purpose of this communication to report some of the cases which indicate, it is hoped, a new development in our present plan of teaching operative surgery; for latterly as the work has been conducted, it has necessarily subjected vagrant animals to the risks and discomforts attending more or less serious surgical procedures carried out for the relief of merely hypothetical maladies.

Four years ago an effort was made in our medical school —and so far as I know for the first time in any school—to change in a radical way those methods of conducting an operative course, which, for the past generation, have been widely adopted and generally regarded as most practicable by the surgical teachers in the leading medical institutions.

Heretofore it has been the universal custom, I believe, whenever anatomical material has been sufficiently abundant to justify its being shared by the clinical departments, to employ the human cadaver for the practical teaching of operative handicraft. And though the opportunities thus offered are admirable in many respects the method is open to serious objections. If I may judge from my own experience not only as a participant but subsequently as an onlooker at these exercises, the students are usually coached in the performance of the more or less stereotyped operations principally on the head and extremities,—the various time-honored amputations, excisions of bones and joints, set ligations of vessels, etc., etc.,—and thus it is the perfected *operation* rather than the *method of operating* upon which chief emphasis is laid.

A course of this kind, in which students are called upon to play an active part, may be not only an excellent surgical supplement to the study of human topographical anatomy but is useful, too, as an introduction to the handling of the surgeon's tools,—still it seems to me that the one great essential of modern surgery is conspicuously wanting. The paramount call upon the instructor, in this Listerian era, is that he shall emphasize and drill into his students, not as mere onlookers or hearers but as actual performers, the significance of that much-abused term surgical "technique," of which to-day the all-important element is asepsis—the first and the everlasting thing to be indelibly stamped on the make-up of everyone who proposes to undertake operative work whether as a surgeon or investigator. Surgical cleanliness, which must become a reflex matter—an operator's second nature—and which, like all other reflexes, must be learned early, is necessarily disregarded in the time-honored methods of teaching this branch in the most unsurgical surroundings of a dissecting room. Next in importance to the acquirement of this reflex habit of cleanliness is the ability to dissect and to gently manipulate living tissues without so damaging them as to interfere with perfect reactionless healing; and a third great requisite, which cannot be learned upon the cadaver, is an acquirement of skill in the proper control of hæmorrhage from the large as well as small vessels, for the old-fashioned rough methods of hæmostasis happily are still followed by few. Nor, finally, can facility in the particular technique of visceral surgery, whether abdominal, thoracic, or intracranial, be properly obtained through practice on the lifeless body, a fact which almost all of those who have been pioneers in these fields of work have emphasized.

With these ideas in mind, our present course of operative instruction was first started upon living animals, stray dogs being used for the purpose, and so far as our opportunities permitted, all of the formalities, that would be observed in regard to a patient admitted for treatment to the surgical wards of the hospital, have been followed. Clinical histories, of which examples will be shown you, have been kept on regular hospital history sheets; the effect of the anæsthesia on the pulse and respiration has regularly been recorded; the detail of the operative preparation both for the staff and patient has been followed; pathological and post-operative notes made; and in case of a fatality, a formal autopsy performed and its results added to the record.

The work has proved so interesting to the instructor and seemingly so acceptable to the groups of undergraduates and graduate students, to whom it has been possible to extend it, that it is gratifying to learn of the establishment, in several other institutions, of courses modeled on similar lines. Our aim has not been to turn out a multitude of operating surgeons, any more than the aim of the manual training departments in some of our modern schools is to turn out finished cabinet-makers or iron-workers, but rather to teach the proper use of the hands and respect for the materials on which they work, through simple actual problems, so that not only may all understand the way work is done and appreciate good work when it is done, but also the few, who are by nature best fitted, may learn of their special aptitude for this particular form of handicraft and be encouraged to continue with it.

After a course of training of this sort and with an acquirement of proper surgical reflexes, a student, when his turn comes, should be found a safe and valuable helper in the hospital operating room where blunders in technique must not

occur; and furthermore he may with profit to himself be an understanding onlooker at the surgical work of others, an occupation, which, for those who have never taken part in or conducted operations themselves, must be granted to be a comparatively fruitless expenditure of time.

For the carrying out of our plan of work, it has been necessary to assume lesions, for the relief of which operative therapy was appropriate—a stricture of the œsophagus, for example, which called for a gastrostomy of one form or another. And it has been our custom, in order that the students, just entering upon their first year of clinical instruction, might become familiar with actual cases rather than their text-book presentation, for them to select from the hospital records cases that were supposed to represent the clinical condition of the animals presented for operation.

We have endeavored to combine this instruction in operative work with the necessary experimentation of the various laboratories, so that, for example, when a gastric fistula was needed in the physiological department, for the study or demonstration of the gastric secretion, the gastrostomy patient mentioned above would suffice, and thus a double purpose be served, with a possible sparing of animal life. The surgical share, also, in many experimental investigations has been undertaken at the same time that the students are learning how to operate—how to handle the tissues and to work with gloved fingers, how to tie and to sponge, how gauze should be used in "walling off" the peritoneal cavity, how incisions should be made and how closed, and a multitude of other things, not the least of which is the proper feeling of responsibility for the general welfare of the anæsthetized patient.

Though satisfactory enough in its ends the benefits arising from such a course are confined to the class and the preceptor and are entirely at the expense of the animal. There is naturally a feeling of regret in the minds of many—of none greater than our own—that animals, particularly dogs, should thus be subjected to operations, even though the object be a most desirable one and accomplished without the infliction of pain, and did expense permit, we would gladly have used animals with which there is an association of less acute sentiment on the part of all. This feeling in the past few months has been somewhat mitigated by the fact that, learning of our work, the owners of animals actually suffering from maladies of a surgical nature, and maladies which most veterinarians are loth to operate upon, have begun to bring these animals to us for treatment, so that there is promise of a clinic, which may furnish us with enough material to obviate in large measure the need of using normal animals.

The surgical report of some of these cases will be made by Messrs. Beall, Faris, Ortschild, and Thacher and it can be seen why the title of Comparative Surgery has been chosen for this report. In the past the work has been conducted at a great disadvantage owing to our cramped quarters, and though every effort has been made for the comfort of the animals before and after the operations, not until the completion of the building, now being erected, will it be possible to give them the real hospital care and accommodation which they deserve.

TWO CASES OF HÆMORRHAGIC CYST OF THE THYROID GLAND.

By C. M. Faris.

Case I.—*Large tumor of the right thyroid gland.*

The patient, a valuable and well-bred, Irish-setter dog, actively used every season for field work, was brought to us for operation by Dr. Cox in March, 1899. On the right side of the neck, in the region of the thyroid, was a tumor measuring on its surface about 8 by 12 cm. (Fig. 1). The time of its first appearance was not ascertainable. The growth has progressively increased in size and of late has greatly interfered with respiration. The mass was very hard to the feel, roundish in outline, with a smooth surface, and so tense as not to impart to the fingers any sense of fluctuation. It was quite movable from side to side, though not



Fig. 1.—Profile view of cervical tumor in Case I.

in an up and down direction. Pressure against the tumor made the animal breathe with a marked inspiratory effort; but without such pressure and when the animal was quiet, there was no evidence of dyspnœa. The right pupil was contracted.

Operation.—March 6, 1899. Ether anæsthesia. *Extirpation of gland and cyst.*

The usual transverse incision (Kocher), with its convexity downward, was made over the tumor. The outer capsule was exposed after division of the platysma and anterior thyroid muscles. The tumor was found to be very adherent, vascular, and its enucleation proved most difficult. It was necessary to divide the right sterno-mastoid muscle and even with this exposure, in the efforts to separate the cyst from the surrounding tissues, it ruptured and several ounces of dark grumous blood-clot escaped. The tissues became so stained that a clean dissection and individual ligation of the groups of thyroid vessels were precluded. Before the mass was finally freed there had been hæmorrhage from several large vessels that had been divided before they could be recognized and secured with clamps. The enucleation was finally accomplished; the divided muscles were reunited with fine silk and the skin closed with a subcuticular silver suture. No drainage was used. An intravenous saline infusion was given.

The animal made an uneventful recovery. The wound healed per primam.

Subsequent History.—The animal lived until the autumn of 1904, four and one-half years after the operation. Death was said to be from old age. His shortness of breath had disappeared after the operation, and for several seasons he proved as useful as ever before as a field dog.

Pathological Report.—The specimen is a large roundish thick walled (1 to 2 cm.) cyst, containing a pasty, grumous, brownish-red material. Its outer surface shows a somewhat shredded fibrous capsule over which lie a number of very large blood-vessels. The inner surface of the cyst wall is divided into irregular spaces by numerous trabeculæ. On section, the walls are found to be made up of several concentric more or less distinct layers, some of which are fibrous and tough, others more friable, having in places the color and appearance of normal parenchyma. Scrapings from the latter show epithelial cells with large vesicular nuclei. Examination of the contents of the cysts showed cholesterin crystals and degenerated blood-cells.

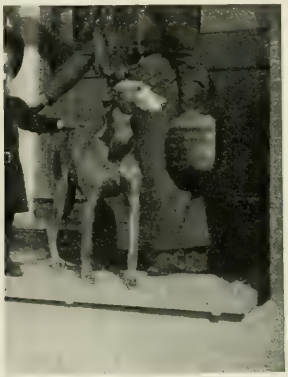


FIG. 2.—Anterior view of cervical tumor in Case II.

The microscopical findings will be described below.

CASE II.—*Large tumor of the right thyroid gland.*

A large, thoroughbred, Russian-greyhound bitch, nine years of age, was admitted in March, 1904, with the following history:

She was a house pet and, having been spayed when four years of age, had grown very stout. Her health had been good until the past year when the present tumor started to develop. For several months she has been dull, inactive and irritable. She occasionally snaps when at play with the children, a thing which never occurred before. There has been some muscular twitching. She has grown very fleshy, has lost most of her hair, and the skin has become dry and scaly. There has been considerable distress for breath, with sighing and wheezing sounds particularly noticeable during her sleep, which is very restless.

Examination.—The pulse rate is 60; the beats irregular in rhythm and quality. No definite exophthalmus is present though the eyes have the usual prominence characteristic of the hound. The right pupil is much larger than the left: both react normally to light. Her skin is rough and scaly though there is no eruption suggesting a cutaneous disease. She has lost most of her coat. She is very fat, and must weigh nearly 100 pounds.

On the right side of the neck, in the region of the thyroid gland, is a swelling about the size of a base-ball; its surface is smooth, almost spherical in outline (Figs. 2 and 3). It gives no sense of fluctuation nor is there any bruit or pulsation.

Considerable interest was aroused as to the diagnosis in this case. The tumor, prominence of the eyes, irregularity of the pulse, nervousness and irritability were suggestive of exophthalmic goitre. Myxœdema was suggested by the change in the nutrition of the skin, the loss of hair, the increase in weight as well as the mental and physical inactivity. The animal however had been spayed and was reaching an age when dogs are liable to show such changes of coat and form.

Operation.—March 12, 1904. Ether anæsthesia. *Enucleation of right thyroid and cyst.* The operation was conducted as in the former case and almost the same difficulties were encountered owing to the vascularity of the tumor and the adhesions about the capsule. In spite of all care, the cyst, as in Case I, ruptured during the manipulations of the tumor. Enucleation was finally accomplished. The left lobe of the thyroid was inspected and seemed normal in size. The wound was closed with silver as in the case above. Healing was absolutely without inflammatory reaction and recovery was uninterrupted.

The animal lived for about a year after the operation, when at her owner's request and owing to her poor physical condition, she was chloroformed. Though for a time after the operation her respiration had seemed to improve and her tremors to be less, the general nutritional state was not altered. The condition of the skin became worse; a cataract developed in the right eye. There were distressing attacks of paroxysmal dyspnœa with an extraordinary depression of the intercostal spaces during the inspiratory act. Thyroid extract was administered for some time before her death without bettering her condition.



FIG. 3.—Profile of neck in Case II. Owing to the extended position of the neck the tumor is less prominent than it otherwise appeared.

Pathological Note.—The gross appearances of the tumor removed at the operation differed but slightly from those of the tissues described under Case I. There is the same thick walled cyst, which, when collapsed and after hardening, measures 8 by 6 by 4 cm., and which contains the same dark reddish, friable, grumous material. The surface of the cyst wall on section presents a laminated appearance, with superimposed fibrous layers between which can be made out, in some areas, narrow strips of thyroid parenchyma. Several small cysts, the larger of which measures 1½ cm. in diameter are to be seen in the surface of the section. No parathyroids can be found.

Microscopic Examination of the Hardened Tissue.—The wall of

the cyst is for the most part made up of dense fibrous layers, between which, in places are zones of glandular substance. The cyst content is made up of a granular, faintly staining mass in which the shadows of blood corpuscles and cholesterin crystals are to be made out. Organization of this clot has begun to take place in some areas along the inner wall of the cyst, where new formed granulation tissue is more or less abundant. Such of the parenchyma of the gland as is still preserved, is altered from the normal. The vesicles, which are still recognizable as such, by their structure and colloid content, are much deformed, most of them being compressed into flattened figures that lie concentric with the curved layers of the cyst wall. Others of them have a crenated outline from the irregular incurving of the epithelial lining. Some of them are partly filled with blood and contain crystals as well as desquamated epithelial cells. The epithelium which remains, is for the most part fairly typical in appearance, though the cells seem less high and contain less protoplasm than normal. In some areas the parenchymal cells are so massed as to have lost all resemblance to their proper glandular arrangement. There is no colloid in these areas, and they are traversed by blood-vessels having extremely delicate walls.

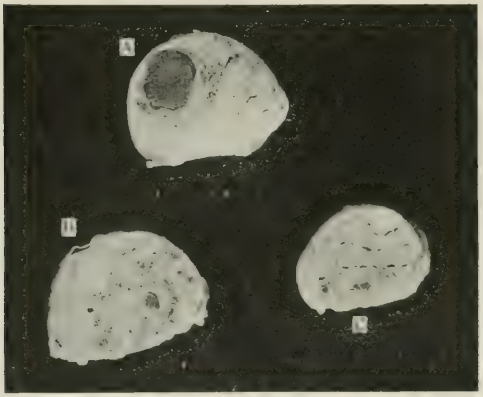


FIG. 4.—Slightly magnified photographs of three cross-sections of the hardened left thyroid gland removed at autopsy from Case II.

The letter *A* is placed near a hæmorrhagic cyst filled with recent clot; *B* is near a large intramural parathyroid body; *C* near a partially absorbed clot, the thick wall of which consists of compact parenchymal cells.

Autopsy.—February 10, 1905. On opening the body the musculature was found to be pale, the panniculus abundant. The abdominal and thoracic viscera were for the most part normal. The lower intestine was injected and on opening the bowel, a hæmorrhagic enteritis extending from duodenum to anus was found. The ovaries were absent; the uterus much atrophied. A large cyst was present in the lower half of the left kidney. These organs, as were the adrenals, spleen, liver, pancreas, and stomach, were otherwise normal on section. There was no glandular enlargement. The heart and lungs were normal except for the presence of a few calcareous nodules scattered throughout the latter. There was no thickening or sclerosis of the aorta. The brain and cord were normal aside from the thickened and adherent membranes characteristic of an old animal.

A careful dissection of the neck was made. No remnant of the thyroid was found on the side (right) of the old operation; nor were there any parathyroids to be found. No accessory thyroids were found in the mediastinal spaces.

The remaining thyroid gland, on the left, was found to be much larger than normal. It measured nearly 6 cm. in its long axis, and its transverse diameters on section were 2 by 1½ cm. The section showed numerous small cysts, the largest measuring about 5 mm. across, and containing a small blood-clot (Fig. 4, *A*). One large parathyroid was present on the surface, equatorial in position, and the section subsequently showed another buried in the substance of the gland (Fig. 4, *B*). There were no polar parathyroids to be found. Microscopical examination of the liver, spleen, kidney, adrenal, and intestine added nothing to the knowledge gained by the gross appearances.

Sections of the thyroid showed alterations varying all the way from the normal, or nearly normal, to the profound changes that had been found in the cyst wall of the gland extirpated the year before. The various compartments of the gland were fairly well

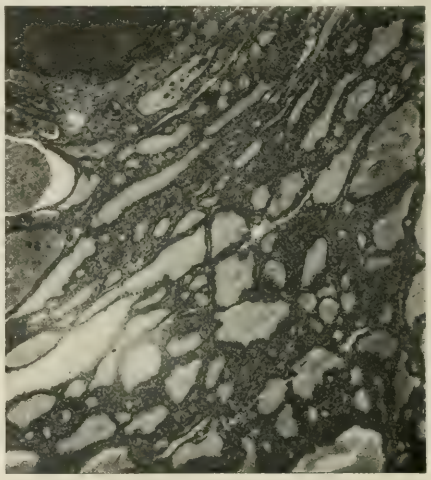


FIG. 5.—Microphotograph of section on the edge of a small organizing hæmorrhagic cyst (left upper corner). Showing compression of neighboring vesicles and hypertrophy in adjoining part of gland.

outlined by delicate fibrous trabeculæ. In some of these compartments the colloid containing vesicles were quite well preserved and lined by a single layer of low epithelium. More commonly, however, the epithelium was infolded and the cells higher in form, while between the vesicles there was a marked cellular proliferation (Fig. 5).[1] This process had gone on in some places to such an extent that in some fields the infolding was so extreme and the multiplication of cells so great, that with the absence of colloid almost all trace of glandular arrangement was lost (Fig. 6). The appearances were closely akin to those seen in experimental thyroid hypertrophy or in advanced stages of exophthalmic goitre.

In some of the compartments of the gland (there were four or five of them), hæmorrhages had occurred (Fig. 4, A) so that it

[1] This, as well as the following microphotographs, has kindly been taken for us by Mr. T. M. Wright, Jr., a simple microscope and ordinary camera being used for the purpose.

was possible to see in miniature just what had taken place on a large scale in the hæmorrhagic cyst removed at operation. The extravasation seemed to have occurred in the central part of the lobule. This had distended and led to a thickening of the lobular fibrous capsule within which the parenchymal cells were massed and crowded together as a lining zone. Occasionally a flattened vesicle was to be seen containing colloid but for the most part the glandular structure in the zone lining the clot was completely lost. In two of the cysts, apparently those of longest standing, granulation tissue was growing out into the clot and large epithelioid cells filled with pigment were interspersed among the inner layer of parenchymal cells. In two of the cysts no effort at repair had taken place, the clot being sharply defined against the compressed glandular acini of the lobule and less evidence of the neighboring hypertrophic change had taken place in these instances.

A large parathyroid was found embedded in the substance of the gland near its middle, (Fig. 4, B). This, as was the case

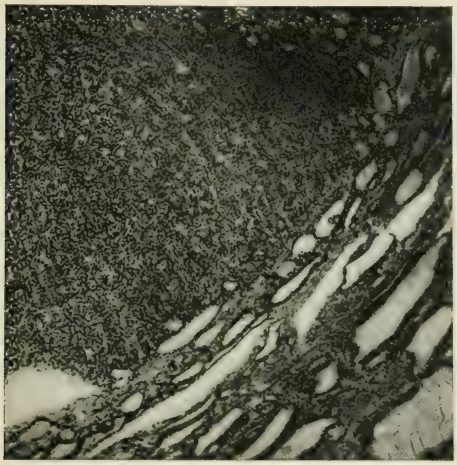


Fig. 6.—Edge of cyst shown in gross in Fig. 4, *C*. Showing zone of compact parenchymal cells.

with the surface parathyroid, showed no apparent alteration from the normal.

Discussion.

Pathological changes in the thyroid gland of dogs are closely analogous to those occurring in man which are better known since they have been subjected to more careful study.

Aristotle, Pliny, Galen, and Aetius are said [2] to have mentioned swellings, which appear to have been goitres, in the necks of animals. Pliny even suggested that the animal's water supply might be responsible for the condition; an hypothesis supported by more recent writers, some of whom without success, have essayed to produce the malady in normal animals by administering in abundance the salts cantained in the water from those localities where the disease is most common. Particularly in certain parts of Europe, goitre is of as common occurrence in the lower animals, more especially horses and dogs, as it is in man himself. It is known in non-domesticated animals, as well. One writer is said to have described a new species of antelope, the distinguishing feature of which was a prominence of the neck which appeared with striking constancy.

The prevalence of goitre is especially noticeable in certain localities, whether from hereditary or geographical influences. Adami [3] has called particular attention to this in describing the so-called goitre regions of Canada and the continent of Europe.

As the pathological and ætiological factors seem to be so closely akin in man and animals, and as the veterinary literature on the subject is difficult of access, we will not limit ourselves to a consideration of the comparative pathology alone.

Simple cysts, as is well known, are of common occurrence in parenchymatous enlargements of the thyroids. The hæmorrhagic variety however is comparatively infrequent. Cysts, apparently of hæmorrhagic origin, have been found by Dr. Bloodgood among the thyroids from the surgical department. But no instance of a large encysted clot such as occurred in our two cases has been met with. They are, however, not unknown. Thus, Bradley [4] has described cases from Dr. Shepard's service in the Montreal General Hospital, some of them the exact clinical and pathological counterpart of our canine cases.

Many conjectures have been advanced in explanation of the way in which these hæmorrhagic cysts are produced. Though trauma may play a part, the predisposing elements are undoubtedly attributable to vascular changes. Thus, Witzel, noticing the ease with which the vessels of the thyroid were torn during operations, suggested that some structural alteration in the vessel wall, possibly a degenerative change, might be responsible for the hæmorrhage. Farner noticed that the ruptured vessels sometimes tore longitudinally. Budde observed that, in cystic thyroids, the smaller arteries showed a connective tissue increase in the sub-endothelial layer without an increase in the intima; also that a degenerative process was demonstrable in the elastica, expressing itself as a separation of the internal membrane of Henle. This was often associated with deposits of calcium salts and as the process occurred in subjects too young for sclerosis, it was considered ætiologically significant in explaining the fragility of the vessels described by Witzel and Farner.

König, in speaking of the hæmorrhagic cysts, calls attention to the extreme dilatation that may occur in the vessels of the thyroid—the so-called Struma aneurysmatica,—in which the vessels may form cirsoid aneurysms in the parenchyma, the veins themselves forming small cysts. Owing to an increase in the size of the vesicles, the supporting connective tissue

[2] A. T. Sloan, Goitre in Animals. The Lancet, Lond., 1887, Vol. I, p. 1802.

[3] Adami, On Ætiology and Symptomatology of Goitre. Montreal Medical Journal, 1900, Vol. 29, p. 1.

[4] W. I. Bradley, On Hæmorrhagic Cysts of the Thyroid Gland. Journal of Experimental Medicine, 1896, Vol. I, p. 401.

network, in which the blood-vessels run, is pressed upon with resultant nutritive changes. The walls of the vesicles become weakened, coalescence takes place between them, and in this way colloid cysts result and may increase to almost any size. Secondary hæmorrhage, occurring through the weakened and perhaps varicose vessels, would give the type of cyst and cystic content that characterizes these cases. The cysts, however, may not always be lined with thyroid epithelium, as might be expected if this were their method of formation, and Wölfner has on this ground been led to reject this theory in consequence. An extensive hæmorrhage, however, might easily spread to the capsule of the gland and only leave a trace of the original parenchyma as a shell on one side of the cyst the walls of which become gradually thickened by new formed tissue. This was the condition found in the two large cysts of our dogs, but in the small hæmorrhagic cysts in the left lobe of the last case, the clots were entirely surrounded by the compressed interlobular parenchyma. It is noteworthy too that in this gland there were no non-hæmorrhagic cysts whatever. We are inclined to agree with Bradley in the view that the cysts originate from the rupture of the intralobular blood-vessels primarily, and that the hæmorrhage may break into or separate and compress the interlobular vesicles.

The contents of these cysts may vary from pure blood mixed with thyroid secretion to dark grumous material, such as we have observed, containing pigment, cholesterin crystals, fat globules, and coagulated necrotic material. Papilloma have been described as occurring within the cysts, but Bradley thinks they are due to irregular infoldings of the walls rather than to neoplastic formation. The great increase in size that takes place in some cases is probably due to repeated hæmorrhages. Doubtless the epithelium lining the cyst ceases to secrete, is soon replaced by granulation tissue and plays no part in the tumor growth.

These cysts, when small, may become cicatrized through organization of the extravasated blood or the clot may remain in an inspissated condition for many years, as in our two cases, with a possible increment from time to time through fresh bleeding. In long standing cases the walls may become calcified or, according to some reports, even ossified. Suppuration of the contents may follow an infection. They may be found in either lobe and, indeed, there are reports of their occurrence in the accessory lobes of the thyroid. In one case of this sort, the writer, Pollard, thought the cyst had occurred secondary to a papillomatous growth.

The interesting complex of symptoms, in our Case II, had it not been for the animals old age, might have been mistaken for the clinical manifestations of myxœdema, for they closely resembled the symptoms shown by an animal after an experimental extirpation of both thyroids, a physiological sufficiency of parathyroid tissue having been left intact. The inefficacy of the treatment with thyroid extract, however, made this improbable and the post-mortem findings showed that the remaining gland possessed an abundance of actively functionating parenchyma. The changes in this remaining lobe, aside from those secondary to the cystic processes, were closely akin to those brought about by physiological hypertrophy, such as Dr. Halsted[5] has described, and which takes place in the portion of gland remaining after partial extirpation.

A REPORT OF TWO CASES OF UTERO-VAGINAL PROLAPSE.

By H. C. Thacher.

Case I.—*Acute descensus of uterus, bladder, and vagina during parturition.*

The patient, a large animal, of mongrel fox-hound type, was operated upon as an emergency case, November 1, 1904. She had received, three weeks previously, when early in her pregnancy, cancer transplantations in both inguinal breasts from the first of Mr. Ortschild's series of tumor cases. The wounds healed per primam and she had since been well and running free in the yard.

Present Illness.—So far as can be told, the animal reached her full term of pregnancy three days ago (October 29), when by her actions she was supposed to be in labor. She did not, however, succeed in delivering her pups and, seemingly as the result of the frequent efforts at expulsion, an œdematous mass began to protrude from the vagina. This prolapse has increased greatly in size and has apparently implicated the bladder, judging from the frequent efforts to micturate.

Examination.—The patient is a full grown, well-nourished animal with a greatly distended abdomen and lactating breasts. She looks sick, shivers almost constantly, and crouches frequently in a straining posture. Her pulse and respiration are rapid.

Protruding from between the labia majora is a large, pendent, rounded mass, measuring about 12 by 6 by 8 cm. Its surface is smooth, moist, cold to the touch; and the fundus of the protrusion is purplish red in color, suggesting almost complete strangulation. On the dorsal surface of the tumor appears the ring-like external os of the uterus. The tumor fluctuates on palpation. It does not seem to be painful or tender.

The animal was prepared for immediate operation as it was conjectured that one of the pups had become fixedly engaged in the superior strait.

Operation.—November 1, 1904. Ether. *Reduction of prolapse: total hysterectomy.*

On opening the abdomen, an enormous pregnant uterus was exposed. This was drawn out of the wound; the broad ligaments were divided and the two horns liberated. The lower part of the right horn was found to be softened and gangrenous. It was torn during the manipulations, disclosing a macerated, foul-smelling fœtus whose head was engaged in the pelvic inlet. The uterus contained eight other living, full-term puppies. By exerting traction upon the body of the uterus, aided by pressure against the prolapse externally, the latter was gradually reduced. Not until this was accomplished did the bladder become visible within the abdomen.

The uterus was then amputated as near the vagina as possible and the stump, after inversion and suture, was ventrally fixed in the parietal wound during its closure.

The animal survived the operation only twenty-four hours. The chart of pulse and respiration, kept during the anæsthetization, shows that the operative procedure was badly borne.

[5] An Experimental Study of the Thyroid Glands of Dogs, with Especial Consideration of Hypertrophy of this Gland. The Johns Hopkins Hospital Reports, 1896, Vol. I, p. 373.

Autopsy.—November 2, 1904. Nothing was found at the examination to account for death, beyond a slight localized peritonitis about the stump of the uterus and a considerable degree of hydronephrosis. The ureters and pelves of the kidneys were all dilated. There was no deformity of the pelvis. No cultures were taken.

CASE II.—*Recurrent vaginal prolapse, unassociated with pregnancy.*

An animal of Irish-setter type, two years of age, was admitted for treatment January 5, 1905, with the complaint that an irreducible mass was projecting from the vulva.

Past History.—She has been a pet dog; has always been well and had the best of care. Owing, possibly to lack of regular exercise, she has grown very heavy. She has never been pregnant. In July, 1904, she was lined for the first time and subsequently suffered from a prolapse of the vagina. The protrusion was successfully replaced by her owner and did not reappear for six months.

Present Attack.—About three weeks ago, without assignable



FIG. 7.—Recurrent vaginal prolapse; condition before second operation.

cause—other than that she was at the time in heat—the prolapse recurred. The protrusion has resisted several forcible attempts at replacement and has gradually increased in size. It is a constant annoyance to the patient though it has seemingly in no way interfered with her health or activity.

Status Præsens.—The patient is a large well nourished bitch, weighing between 15 and 20 kilograms. Her general condition is excellent and aside from the local trouble, the examination proves negative.

Projecting from between the enlarged labia majora is a smooth, tense-looking, rounded mass, about 25 cm. in circumference and 7 cm. in length (Fig. 7). Upon the upper and posterior aspect of the protrusion lies the opening of the inverted vagina. The cervix uteri cannot be reached by the finger introduced within this opening. The greater part of the protrusion is covered with a somewhat congested, granular and thickened mucous membrane. On the lower aspect of the mass—that which comes in contact with the ground when squatting—there is a large superficial ulceration covered with a greyish slough. The tumor has a tough, boggy, œdematous feel and is cold to the touch though its circulation seems good. The orifice of the urethra is drawn down into view on the anterior aspect of the neck of the tumor.

Diagnosis.—Prolapsus vaginæ et vesicæ.

Operation I.—January 6, 1905. Preliminary morphia; ether anæsthesia. *Reduction of prolapse. Abdominal hysterectomy. Ventral fixation of stump.*

While the animal was being cleaned up for operation, an effort was made to reduce the prolapse; this was unavailing even with complete muscular relaxation under the anæsthetic and with the hind-quarters elevated. The abdomen was opened by an 11 cm. intermuscular incision, through the inner margin of the right rectus. After exposure of the uterus, a long, steady traction upon its body brought about a partial reduction of the prolapse, the manipulations succeeding in drawing into the abdominal cavity the bladder whose walls were very much congested. Complete reduction, however, was only attained after combining pressure from without with the traction upon the uterus. After the reduction the uterus was drawn well into the wound, was amputated close to the external os and its stump was amputated and inverted with mattress sutures. The broad ligaments were then divided, the uterine horns freed from their ovarian attachments and the entire uterus removed.

The abdominal wound was closed in layers, the stump of the vagina being drawn up and securely fastened to the posterior sheath of the rectus in the hope that this would suffice to prevent a recurrence of the prolapse. The relaxed vaginal canal was packed with iodoform gauze.

Post-operative Note.—On the following day the prolapse was found to have recurred in its original form and was, if anything, even larger than before. There were otherwise no complications following the operation. With the exception of a single slight stitch abscess, the abdominal wound healed per primam.

Four weeks later a second and successful operation was conducted, as follows:

Operation II.—February 3, 1905. Preliminary morphia; ether anæsthesia. *Combined abdomino-vaginal operation. Amputation of prolapse by Whitehead's method for rectal prolapse.*

The abdomen was reopened in the line of the original incision. The stump of the vagina was freed from its attachments to the abdominal wall; the bladder was, this time, found in place in the abdominal cavity. On catheterizing the urethra, it was ascertained that a loop of this canal was drawn down with the prolapsed tissues into the neck of the tumor. By introducing a straight catheter into the bladder it was possible to place the urethra in a position where it was unlikely to be injured in the proposed operation.

An incision was then made encircling the neck of the prolapse about at the junction of the vulvo-vaginal mucous membrane and just so as to escape the urethral orifice. While the tumor was grasped and drawn away from the body, this circular incision was gradually deepened with the knife and by blunt dissection—the large vessels being secured as they were encountered—until the sub-mucous coat of the non-inverted portion of the vaginal canal was reached. The vagina, at this situation was then amputated section by section, as its edges were sutured securely to those of the vulval side of original incision. The abdominal wound was then closed as before with fixation of the vaginal stump in the parietal wound.

Convalescence was without incident. As after the first operation the ventral wound healed with a single stitch abscess. There has been no recurrence of the prolapse.

Pathological Report.—The specimen consists of a piece of tissue, 10 by 7 by 4 cm., roughly ovoid in shape and obliquely traversed by a lumen about 2 cm. in diameter. The tissue is firm and elastic in consistency. The outer surface is, for the most part, covered with mucous membrane which passes into the lumen above described. The surface is brownish red in color, somewhat granular and at one point slightly ulcerated. Within the lumen the mucous membrane is pink and smooth. On section the tissue

is found to be very œdematous and somewhat vascular. It consists of a meshwork of grayish, semi-translucent bands and fibers, the majority of which seem to radiate from the lumen. The sub-mucosa is dense and thickened. The mass weighs 125 grams in its present shrunken state.

Discussion.

Obstetrical complications, as illustrated by the first of these cases, are very common in domestic animals. Upon their occurrence in cattle and horses there is a large literature.[6] It is quite common for animals to die in labor without delivery. This is especially true of dogs.

The acute prolapses, which occur before and during parturition, are more frequently reported in the veterinary literature dealing with cattle—more attention being paid to this animal owing to its greater commercial value. According to Vennerholm,[7] it is of common occurrence in stall-fed and milch cows, particularly in animals standing in stalls with a floor sloping backwards for drainage. In pasture free animals it is comparatively rare. Relaxation of the pelvic floor and an extra large sized pelvic outlet[8] are predisposing factors. An unusually heavy uterus is also recognized as a causal factor and may have played a part in producing the lesion in the first of our canine cases.

As a rule, the prolapse in cattle appears only when the animal is recumbent and reduces spontaneously when the animal takes a standing posture. Rarely does the condition seem to offer any serious obstruction to labor. The usual veterinary treatment is an operative one in case the prolapse does not spontaneously disappear after labor. The procedure consists of the use of metal clamps to close the labia and prevent the descent of the tumor.

Kitt[9] mentions the fact that prolapse is common—especially in animals dying from anthrax or black-leg—as an agonal occurrence.

Case II illustrates a condition much more rare. Some cases of prolapse unassociated with pregnancy, have been reported in young animals—colts—suffering with "colic."[10] Reports of cases in which the bladder has formed part of the prolapse are still more uncommon. Franck recognizes two main types—one with simple inversion of the bladder, the other with its extrusion through the torn vagina. Very little attention seems to have been paid to complications of this nature which have arisen in dogs and the literature upon the subject is scant and inaccessible.[11]

[6] Franck, Thierärzliche Geburtshilfe. Berlin, 1901. DeBruin, Geburtshilfe beim Rind. Wien u. Leipsig, 1897.

[7] Vennerholm in Bayer, and Fröhner's Handbuch der thierärzliche Chirurgie und Geburtshilfe. Wien und Leipsig, 1897.

[8] Streble, Journal of Comparative Pathology. 1901.

[9] Kitt, Pathologische Anatomie der Hausthiere. München, 1901.

[10] Koepke, Berliner thierärzliche Wochenschrift. 1892.

[11] Since writing the above report a third case of prolapse of the nature of this supposedly more rare type, has come under our observation.

A REPORT OF EIGHT CASES OF CANINE NEOPLASM.

By J. F. Ortschild.

Case I.—*Adeno-carcinoma of breast with glandular metastases.*

A small, long-haired, yellow, Skye-terrier bitch, sixteen years of age, a nullipara and a house-pet, was admitted to the clinic in September, 1904.

History.—For the past six years the patient has been kept for the most part within doors and under close observation. Not until two months ago, was a small hard mass noticed in one of the breasts. It has been rapidly increasing in size and has become ulcerated. There is no history of traumatism.

Examination shows a very old, feeble, emaciated and inactive dog. The mucous membranes are pale; only a few loose teeth remain.

In the right, most posterior, inguinal breast, there is an ulcerating, fungated growth, the size of a hickory nut (Fig. 8). The ulcerated surface has, upon one side, an overhanging edge, but

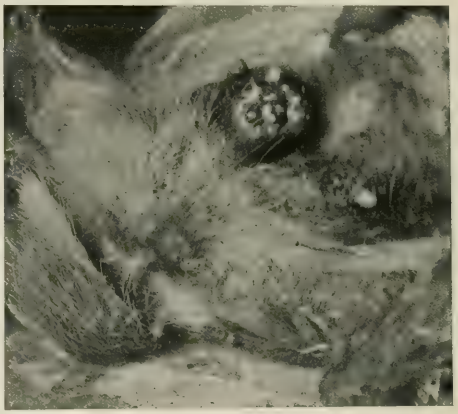


Fig. 8.—Tumor of right inguinal breast of Case I.

there is nowhere any definite undermining of the epithelial margin. The surrounding skin is darkly pigmented. On palpation the tumor is firm and has an irregular, nodular outline. The moist ulcerated surface is reddish in color, with some gray streaks made by superficial sloughs. The nipple does not seem to be involved in the growth, though it is somewhat retracted.

In the subcutaneous tissue to one side of the tumor are three or four hard, freely movable, discrete nodules, presumably involved glands.

Operation.—October 7, 1904. Morphia; ether. *Amputation of breast.*

The breast, the tumor, the glands and the neighboring fat of the inguinal region were removed in one piece, and though the surface of the tumor had been ulcerated, an effort was made to secure primary union and the wound was closed without drainage.

Subsequent history.—The wound broke down in large part and closed slowly by granulation. Soon after the operation an ulcer appeared at the angle of the mouth. This ulcer proved phagedenic, spread rapidly and assumed the clinical appearance of a cancrum oris (noma), finally involving the gums and the adjoining cheek. The patient died from this infection two weeks later.

Autopsy.[12]—October 21. There were no visceral metastases; the abdominal and thoracic organs were practically normal. The eroding ulcer of the mouth had eaten its way into the nasal cavities, which were filled with pus. No cultures were taken.

Pathological Note upon the Tumor.—The mass on section shows a rather homogenous surface, which is slightly moist, of a pinkish gray color, and is flecked with yellowish points, which can easily be scraped off with the blunt edge of the scalpel. The glands are quite deeply pigmented; the deposition of pigment being most marked in the centre. Their appearance led to an operative diagnosis of melanotic sarcoma.

Histologically, the primary growth is found to be in reality a carcinoma. Its most striking feature (Fig. 9), is that of a malignant adenoma, with a stroma infiltrated by glandular elements. The stroma, however, is very cellular, containing large ovoid cells full of brown pigment granules. There are many cysts lined by high epithelium, some of them containing papillomatous growths.

The large metastatic nodule has similar characteristics, the

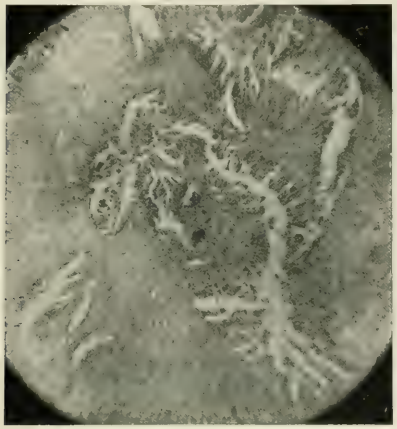


FIG. 9.—Low-power magnification. Showing character of adenomatous growth in primary tumor.

cystic and adenomatous elements predominating (Fig. 10). In the lymph glands containing early metastases, the adenomatous structure is not apparent, the cells making up the area of newformed tissue, being for the most part similar to the pigmented (mesoblastic?) cells of the primary growth (Fig. 11). Diagnosis: Adeno-cysto-carcinoma.

Transplantations from the tumor, immediately after its removal on October 7, were made into three dogs, one of which was practically of the same strain as the original host. Pieces of tissue were transplanted in one animal into the liver and between the transversalis fascia and peritoneum; in another case into the two inguinal breasts, both of which were supposed to be hypertrophied (in reality, as subsequent observations showed us, the prominence of the mammæ was due to underlying inguinal herniæ—compare Mr. Beall's report); in the third, a pregnant animal, a sub-peritoneal as well as a mammary inoculation was made. A portion of the original tumor, as well as a fragment of an involved gland, was used for transplantation in each animal.

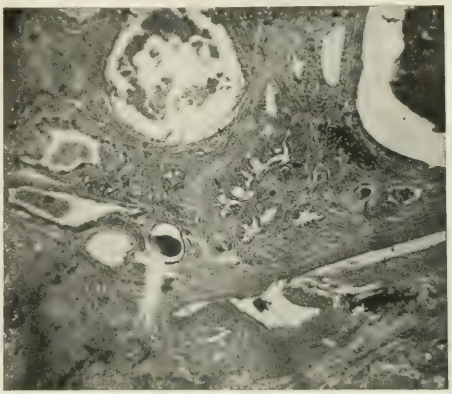


FIG. 10.—Metastatic nodule; field showing glandular and cystic characteristics.

The subsequent history of these animals cannot be entered into here, other than to say, that the third of them is Case I, of Mr. Thacher's series, and that the second was found dead, six months

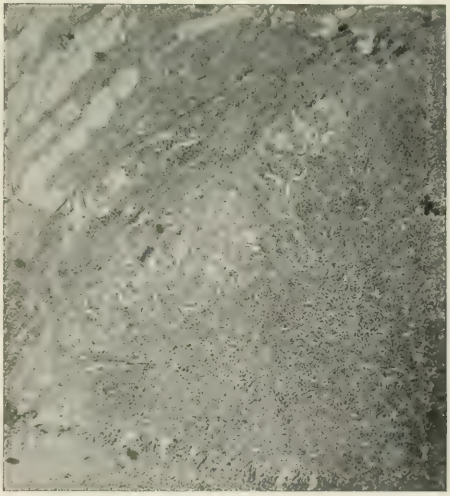


FIG. 11.—Lymph node with very early marginal metastasis.

later, with an increase in size of the piece of tissue transplanted from the tumor into the right breast, and with enlarged and pigmented lymphatic glands in the inguinal region of the opposite side, namely, that into which the fragment of glandular metastasis had been transplanted.

[12] Owing to the length of Mr. Ortschild's report, the post-mortem notes, as well as the histories of the animals that were used for experimental transplantation, must necessarily be greatly abbreviated. It is hoped that his interesting observations may be given more in detail in a later communication. (Cushing.)

CASE II.—*Mixed (teratomatous) tumor of the breast with multiple metastases.*



FIG. 12 (Case II).—Showing situation of primary growth and the palpable metastases. Site of nipples indicated by solid black dots.

A small, gray-haired, Skye-terrier bitch, was admitted January 16, 1905. She had been a vagrant animal and no history was



FIG. 13.—Photograph after patient was shaven in preparation for operation.

obtainable. She was an old dog, though seemingly in good condition; not cachetic nor anæmic. She was evidently a multipara from the appearance of the nipples.

Special Examination.—Scattered about the ventral surface of the thorax and abdomen, are numerous hard subcutaneous nodules, varying greatly in size (Fig. 12). The largest, evidently the primary growth, occupies the second left thoracic breast, on a level with the costal margin. It is made up, seemingly, of a conglomerate mass of separate tumors, forming in all an irregular growth about 5 by 4 cm. in length and breadth, and 3 cm. in thickness. It is freely movable on the underlying tissues; is covered by thin, freely movable skin, under which run considerably dilated vessels. The nipple is not adherent nor retracted. The growth is not sensitive on pressure and is very hard to the feel. From this main growth, a chain of nodules, varying in size from a buckshot to a large pea, spreads across the mid-line onto the right side. Though some of these nodules are fused, they, for the most part, are individually movable. The chief collection



FIG. 14.—Same as Fig. 13. To show prominence of primary tumor and projecting nipple.

of them is clustered into a prominent tumor, almost as large as the primary growth (Figs. 13 and 14). A chain of these nodules, extending up toward the right axilla, can be palpated through the skin of the thorax. Higher up on the left side, above the axillary nipple, can be felt a similar chain. Two other large clusters are present, one over the left pectoral region, and another over the left inguinal breast, which was supposed to be hypertrophied (in reality overlying an inguinal hernia). There are a number of other individual nodules all of which are firm, but without the stony hardness possessed by the primary growth. No masses are palpable within the abdomen.

Operation.—January 16, 1905. Morphia; ether.

Through three separate incisions, the main tumor, together with the second left breast and the surrounding tissue, the mass of discrete nodules, together with the adjoining second right breast, and the larger one of the individual tumors, were removed. The wounds were closed without drainage.

Pathological Note.—The primary tumor presents, in gross, an irregular, nodular surface like that of a compact bunch of grapes. The surface is of a pinkish white color with some few points of hæmorrhage. The rounded nodular projections are smooth and

glistening. The mass is firm and rock-like in consistency. On section, bony resistance is met with, the knife penetrating only with the exertion of considerable force. The surface of the section shows an outer shell consisting of a layer of cancellous bone, varying in thickness from 1 to 2 cm. Radiating from this shell, into the substance of the tumor, are delicate bony trabeculæ, visible to the naked eye. In the central portion are irregular islands of non-calcified tissue. These islands are for the most part, whitish-gray, more or less translucent, and made up of soft tissue. Cartilaginous areas are to be made out.

The metastatic mass and the discrete nodule that were removed, resemble one another on cross section, very closely. They present a very cellular and granular appearance, with a more translucent cortical zone and a dark, pigmented center or medulla. No bony trabeculæ or cartilage can be detected. Some of the nodules are evidently lymph glands containing macroscopical areas of new growth.

Microscopically, the tumor shows, in addition to the bony trabeculæ and cartilaginous areas, that are discernible with the naked eye, that the cellular areas are most diverse in structure

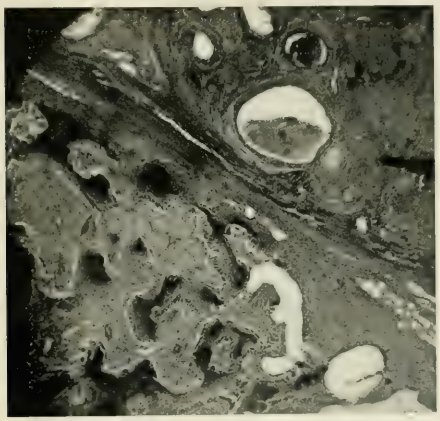


FIG. 15.—Field from primary tumor of Case II; showing bony trabeculæ, separated by a strip of fibrous tissue from an adenomatous area with cyst formation.

(Fig. 15). Some of them are of a pure adenomatous type; others resemble carcinoma simplex. There are fields of closely packed, large, and small round epithelial cells, and in places the loose meshwork resembles embryonic connective tissue. In other places the tumor shows true osteoid tissue. The lamellæ of the bone are uniform, have no Haversian systems, and are lined by numerous osteoblasts. The spaces between these lamellæ are filled with a meshwork of spindle cells in which are also found large cells resembling epithelial cells. Several areas show squamous epithelium. In many places there is no sharp demarkation between stroma and epithelial cells, one being invaded by the other. In the metastases, the neoplastic elements are mainly adeno-carcinoma (Fig. 16), with no cartilage or bone. Were it not for the cartilage and bone, the tumor could be correctly called an adeno-carcinoma.

Transplantations and Injections.—An emulsion of the original tumor was made immediately after the operation by grinding fragments of it in a mortar with sterile salt solution. The pulp thus obtained was used for injections. Portions from the metastatic nodules were similarly treated. This method was followed, owing to the success that has attended it in the transplantation from mouse to mouse of a malignant carcinoma simplex through many generations by Drs. Cloues and Gaylord at the Gratwick Laboratory.

Inasmuch as it was surgically impossible to remove all of the involved nodules from the original host, it was considered justifiable to use this dog for control inoculations from her own tumor. Before she came out of the anæsthetic, therefore, a small portion of the original bony tumor was aseptically inserted under the skin in the right axillary region. A small piece from one of the involved glands was similarly implanted on the left. In addition, 2 cc. of the emulsion from the gland were injected under the skin at the suprasternal notch and a similar quantity of the primary tumor emulsion into the subcutaneous tissue between the scapulæ. Corresponding implantations and injections were made into four other animals. One of these animals, a very old dog, died of an intercurrent infection two weeks later and before any macroscopical growth could have occurred; but in the subcutaneous tissues of this animal, at the site of the inoculations of the glandular emulsion, there were found, microscopically, numerous clusters of viable epithelial cells. The other four of the series

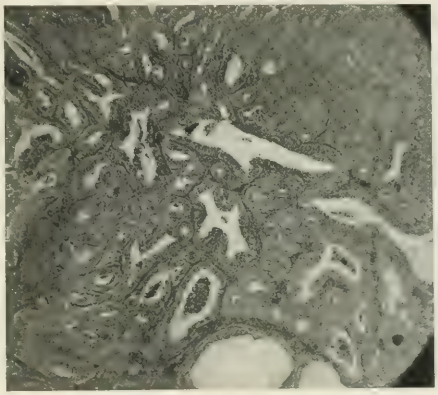


FIG. 16.—Metastasis from Case II. Field showing pure adenoma with cyst formation.

were killed about five weeks later by a vicious bull dog that was inadvertently let into the yard. The bodies were too much mutilated to be of any pathological value, though a fresh series of transplants was made from the remaining tumors of the original host.

CASE III.—*Cysto-adenoma of the breast with metastases.*

A small, short-haired, very stout, almost toothless, decrepit and inactive, old, black-and-tan bitch was admitted for operation, January 16, 1905. She was a vagrant dog without a history. The condition of her nipples evidenced previous pregnancies.

Examination.—In the second left breast, there is a firm, oval nodule, about the size of a pea. There is no retraction of the nipple nor any discharge from it. A chain of three distinct nodules, similar to the above, is present in the second right breast. The nipple is not retracted but discharges a thin, yellowish fluid on pressure. In the third left breast, there is an indistinct mass of very firm tissue, suggesting matted glands. In the third right breast, there is a large oval mass, evidently the primary growth, 2 cm. in length by 1½ cm. in breadth and 1 cm. in thickness. This is firm, though not of bony hardness, freely

movable, not adherent, circumscribed and irregularly nodular. The inguinal breasts are free from nodules but prominent owing to small underlying inguinal herniæ.

Before the patient was subjected to operation, she died from a phagedenic buccal infection that seemed to originate in the gums about her few remaining and diseased teeth.

Autopsy.—January 29, 1905. The largest tumor, upon removal, is found to be irregularly nodular, smooth, encapsulated, and somewhat elastic in consistency. It is generally light in color, mottled with white and dark brown areas. The surface, upon section, is granular and shows the same mottled appearance seen on the outer surface. The metastases have the same general aspect as this primary tumor.

The examination was otherwise negative, except for the presence of calculi in the bladder and urethra and the extensive ulceration of the mouth.

Microscopic examination shows the tumor to be divided into compartments by fibrous bands radiating through it from the capsule. Except that there are no bony or cartilaginous elements discernible, the general structure of the growth is not unlike that found in Case II. The predominating type of tissue is adenomatous. This is cystic in places (Fig. 17). The cysts, some of them very large, are lined by high columnar epithelium and in many cases contain papilliform ingrowths. Many of the cysts—and these have a lower form of lining epithelium—contain a homogenous mass of waxy looking secretion. Some of the areas are densely cellular, having the character of spindle-cell connective tissue. But even in these densely packed fields there are to be made out structures resembling epithelial glands.

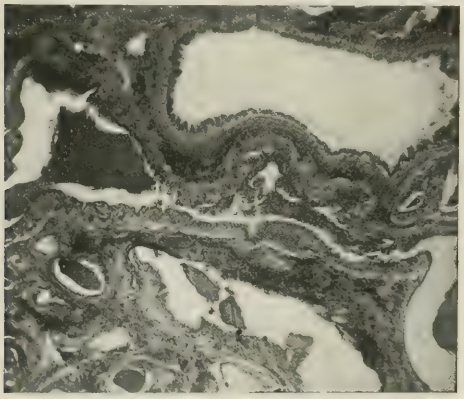


FIG. 17.—Section of tumor of Case III. Showing the more cystic portion of an adenomatous field.

CASE IV.—*Mixed (teratomatous) tumor of the breast with metastases. Lipoma.*

A valuable, black and brown, Gordon-setter bitch, 8 years of age, was brought in by her owner, February 3, 1905.

History.—Until the present trouble developed, she had been a strong and healthy dog, used for active field work. She has had five litters of pups. The last litter was whelped nine months ago. When the pups were a month old, one of them bit the patient in the most posterior right inguinal breast. The breast became sore and a short time afterwards she developed, what her owner calls, "a milk breast." The mass remained small and did not become particularly noticeable until four months ago, but since then it has been enlarging rapidly.

Examination.—The animal has a glossy coat and seems in excellent general condition. In the posterior inguinal region of the right side, between the last two breasts, there is a large irregularly oval mass (Fig. 18), measuring 10 by 7 by 8 cm. The tumor hangs pendent from the abdomen and is freely movable over the underlying structures. The overlying skin, though not adherent, is somewhat thinned out and injected; and at the most dependent part has become abraded leaving a superficial area of ulceration about 4 cm. in diameter. The mass is irregularly, coarsely nodular, for the most part very resistant to pressure, though having several areas which are less firm and suggest the elasticity of tense cysts. The nipples are not retracted nor is there any discharge from them. The inguinal glands are palpably enlarged on this side.



FIG. 18.—Right inguinal tumor in Case IV.

In addition, there is a small mass under the skin of the left pectoral region, oval in shape and about 3 cm. in diameter. It is lobulated, firm, freely movable under the skin, and not adherent to the tissues beneath. The highest nipple on the left, closely adjoining this tumor, is markedly retracted, but the gland itself does not seem to be, in any way, involved by this growth.

Operation.—February 3, 1905. Ether anæsthesia. *Amputation of breasts and tumor.*

The tumor with the two adjoining breasts and involved lymphatic glands was removed in one piece. The broad spindle-shaped opening in the skin was closed without drainage. The tumor over the left pectoral region was similarly excised together with the neighboring mamma.

Subsequent History.—Both wounds healed by primary union leaving almost invisible scars. The patient has remained well.

Pathological Note.—After removal, the tumor presented the same general characteristics described above. The cystic areas were, however, more in evidence especially in the lower and more posterior part of the tumor. The growth on section is found to contain bone, cartilage, cysts, fibrous and cellular areas, all of which are discernible to the naked eye. The dense fibrous

tissue is particularly abundant in the centre of the growth, with bands which radiate out towards the periphery (Fig. 19). Within these septa the more cellular areas have an opaque, yellowish, granular appearance, and upon pressure exude a dirty yellow substance.

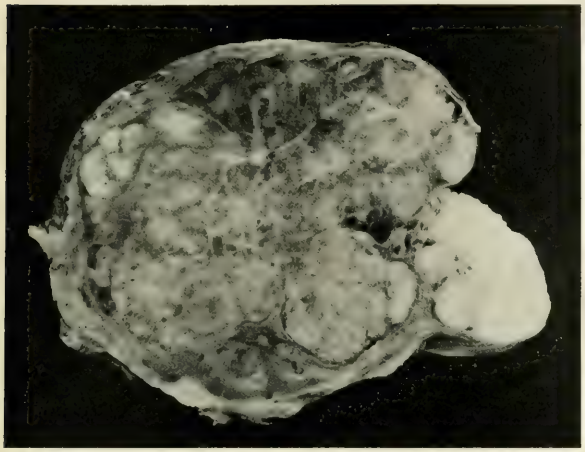


FIG. 19.—Photograph, ¾ natural size, of gross appearance of tumor from Case IV; mid-section showing more cellular part of tumor, no bone or cartilage being visible.

Microscopial examination.—The mass is a mixed tumor, very similar to that of Case II, the description of which might well apply to this tumor. There are found all the areas noted with the naked eye, cartilage, bone, cysts, fibrous and cellular tissue.

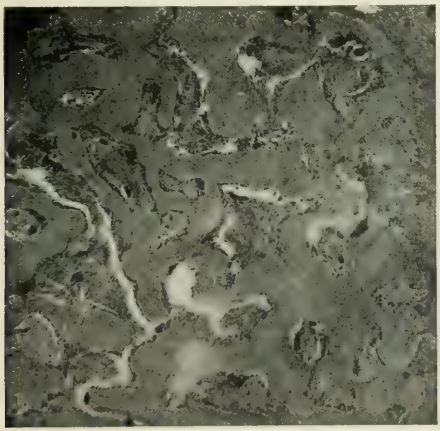


FIG. 20.—Microphotograph of field with bony trabeculæ. Case IV.

Large cystic areas, lined by a low epithelium are found in which a coagulated fluid is present. Other cysts show papillomatous ingrowths. Some areas are purely adenomatous; others are entirely fibrous; while still others show tissue resembling embryonic connective tissue (Figs. 20 and 21). As the adeno-carcinomatous elements predominate, were it not for the bone and cartilage, the diagnosis of adeno-carcinoma would be made.

The small tumor from the left pectoral region, macroscopically, is a fatty tumor, a diagnosis confirmed by histological examination.

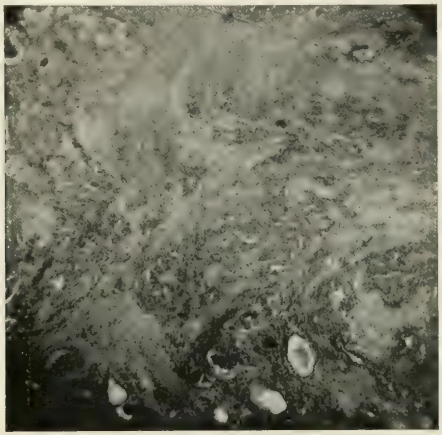


FIG. 21.—Fibrous and cystic area from tumor of Case IV.

Transplantation from the malignant tumor was made into one dog.

CASE V.—*Intra-cystic papilloma of the breast, with metastases.*

The patient, a valuable black, Gordon-setter bitch, ten years of age, was brought in by her owner, February 15, 1905.

History.—She had always been well and actively used as a field dog. When nine months of age she had her first litter of pups. A second litter was whelped three years ago when she was seven years old. One of the pups of this litter in suckling injured the right inguinal breast. Apparently an abscess formed, which discharged pus. This finally healed, leaving a small palpable nodule in the breast. The mass has increased slowly in size up to the present time and has become so large that it incapacitates her from active exercise (Fig. 22). The owner has never noticed any discharge from the nipple.

Examination.—The animal has a glossy coat and seemingly is in the best of condition. In the right inguinal region between the two most posterior breasts, is a large, heavy pendent mass, measuring 10 cm. in length, by 6 cm. in breadth and thickness. It is freely movable over the underlying tissues. The overlying skin is thin and injected but not adherent to the tumor. It is without abrasion. The mass is irregularly lobulated, hard, and firm, but not of bony consistency. There are several softer, elastic and fluctuating areas suggesting cysts. Under the last breast and extending from it towards the inguinal region is a deeper lying soft swelling. The nipples are not retracted. On compressing the tumor there shot out from the inguinal nipple, for a distance of several feet, a fine stream of serous blood-stained fluid.

In the region of the left most posterior inguinal mamma are a number of discrete rounded nodules, varying in size up to 1 cm. in diameter. They are freely movable under the skin and to the feel resemble the firmer areas of a primary growth. The neighboring nipple is not retracted nor can any discharge be

expressed from it. The inguinal glands are enlarged on both sides.

Just posterior to the third and to the fourth mammæ on the left side are two nodules the size of cherries, that possess characteristics resembling those of the firmer portions of the main tumor.

Operation.—Feb. 15, 1905. Morphia; ether. *Amputation of breasts and tumor.* The large tumor with the two adjoining mammæ was removed with a wide margin of healthy tissue. After removal of the tumor and the breasts the deeper lying mass described above was examined and found to be a small right inguinal hernia. This was operated upon by Mr. Beall and is Case III of his series. One of the nodules—that posterior to the third left breast—was also removed, through a separate incision, and the wound closed with interrupted silk sutures.

Subsequent Note.—The wound, made by the larger operation on



Fig. 22 (Case V).—Large pendent tumor at right inguinal breast.

the right side, superficially broke down in part and healed by granulation. The smaller wound healed by primary union. The animal died eleven days after operation from a very virulent infection of the left hind foot.

Pathological Note.—The tumor is encapsulated, of a reddish color, with small somewhat translucent and more whitish nodular areas, varying in size from a fine shot up to that of a buckshot or larger, and surrounded by darker areas. Its surface is very vascular.

Upon section (Fig. 23), the tumor is found to be made up of two more or less distinct areas. The anterior portion consists of comparatively solid tissue, but posteriorly the knife enters a large cyst which contains thin blood-stained fluid similar to that which could be expressed from the nipple before the operation. The cavity of the cyst measures 5 by 4 by 3 cm. Its outer wall is very thick, especially in the most ventral portion, where it measures 2 cm. The wall in these thick areas is mainly fibrous, somewhat firm and elastic, and contains several small, round, yellowish areas.

The inner surface of the cyst wall is very irregular, numerous pockets being formed by the irregularities. The entire right half of the cyst—and to a less extent the remainder—is lined with coarse vegetations. The surface of these fungous ingrowths, some of which are distinctly pedunculated, is coarsely granular and presents a very ragged appearance. The vegetations are reddish in color and lodged between the larger projections are numerous

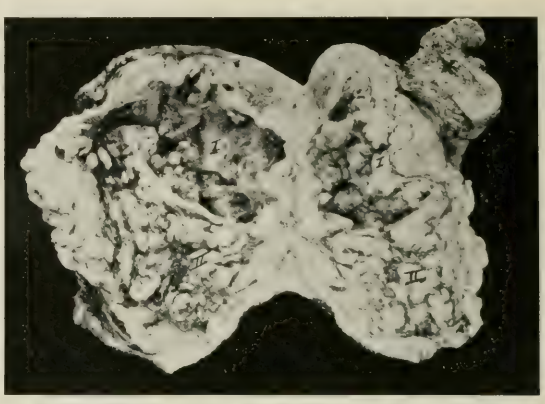


Fig. 23.—Median section of tumor from Case V (½ natural size). Showing cyst with intracystic vegetations in upper half of section (*I*) and compact tissue in lower half (*II*). Breast and nipple (*X*) in right upper corner.

reddish coagula. These papillary ingrowths present, on section, an appearance similar to that of the isolated areas in the cyst wall, as well as that of the more solid portion of the tumor.

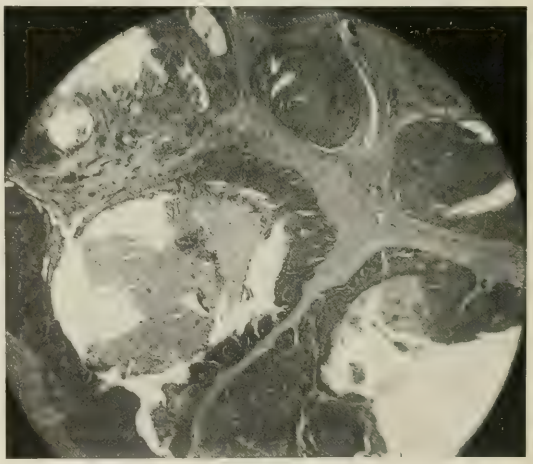


Fig. 24.—Microphotograph of tumor, Case V, showing alveolar arrangement.

This solid part of the growth seems to be made up of compact masses of papilliform growths such as individually project into the cyst cavity. Between the masses of cellular tissue can be made out smooth walled channels, many of them containing shreds of blood coagula. The stalks of the cell masses contain a large amount of fibrous tissue. The cut surface is smooth, moist, yel-

lowish and homogeneous, having a slightly granular appearance. Upon pressure there exudes a thick, semi-fluid, dirty, yellowish substance.

The whole tumor presents the characteristic appearance of an intracystic papillomatous growth. In the still cystic portion of

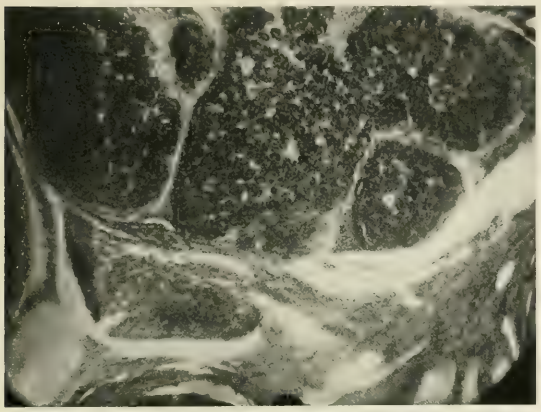


Fig. 25.—Microphotograph of metastasis to lymph gland from Case V.

the tumor the ingrowth only partially fills the cavity. The more solid portion apparently represents a pre-existing cyst that has become completely obliterated by the ingrowth. The metastatic nodule is similar, in all respects, to the solid portion of the original tumor.

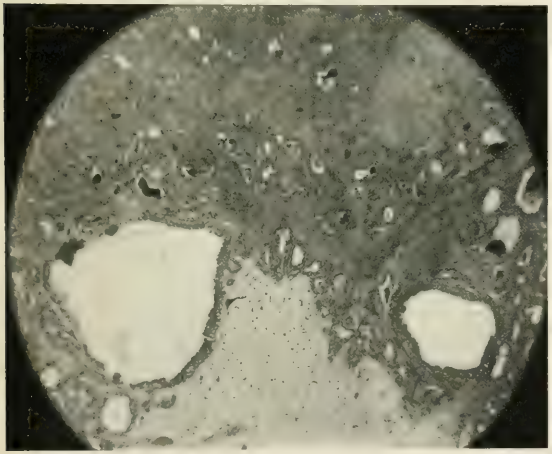


Fig. 26.—Microphotograph of metastatic nodule; field with adenomatous and myxomatous areas.

Microscopical examination shows the tumor to be a very cellular one (Fig. 24). In some areas there are numerous fibrous bands running in all directions, dividing the tumor up into alveoli. In these alveolar areas the epithelial cells are compact, often filling the entire space. In other areas the appearance is adenomatous, while in still others, the appearance is that of intracystic papillomatous growths. The section of the papilliform growths in the large cyst shows them to be almost entirely made up of cells of an epithelial nature, similar to those in the other areas of the tumor.

The metastasis to the lymph gland preserves the general character of the original tumor (Fig. 25). The alveolar arrangement and the papillomatous structure is beautifully shown. The metastatic nodule (Fig. 26) shows dense fibrous bands in places, also large areas of myxomatous tissue in others, and preserves the intracystic and adenomatous character of the original tumor.

Transplantation from this growth was made into two dogs.

Case VI.—*Fibro-lipoma of the vaginal wall.*

History.—Small, fox-terrier bitch, eight years old, a house pet, was brought to the clinic, March 17, 1905. She had her first and only litter of pups seven years ago. Last July a lump, the size of a small pigeon's egg, was noted in the perineal region. This swelling grew slowly at first, but during the last few months has increased rapidly in size. The mass has caused no inconvenience to her so far as the owner has noticed.



Fig. 27 (Case VI).—Showing size and position of tumor. The dilated vaginal opening, blocked by the growth, is visible at the lowermost portion of the tumor in this view.

Examination shows a small, old, active, fox-terrier bitch, very fat and in good general condition. The patient has difficulty in passing water. In the perineal region there is a marked posterior bulging of all structures making a solid mass outside the pelvis, considerably larger than a closed fist. The opening into the vagina is apparently blocked by this mass, a portion of which the size of a twenty-five cent piece, covered merely by mucous membrane, is externally visible through the vulva. This mucous membrane is dark red, hyperæmic and slightly ulcerated. The skin over the mass is not adherent but is thin. The mass seems to project through the pelvic outlet, is circumscribed, very firm, somewhat elastic, and of a tenseness suggestive of a distended bladder such as was observed once in a hernia case. (See Mr. Beall's first hernia case in fox-terrier.) In the anterior area the surface is more irregular. There are no enlarged glands palpable in the groins.

The extraordinary appearance of the mass is shown in the photographs (Figs. 27 and 28). It was supposed to represent a large prolapse containing bladder and intestine.

Operation.—March 17, 1905. Ether. *Enucleation of tumor.* The mass was found to be a large, solid, fibroid tumor of the vaginal wall and was enucleated through a median incision, extending from near the tip of the vulva to the mid-hypogastric region. Under the belief that the abdominal viscera made up part of the supposed prolapse, it was intended to open the abdominal cavity. Not until the tumor was almost entirely enucleated, did it become evident that it had no real connection through the pelvis and could not be other than an isolated growth. It was so definitely encapsulated that, mostly by blunt dissection, could it be freed from the surrounding tissues. Only in one place was it adherent, viz., at the spot where it was covered merely by the exposed vaginal mucous membrane, and owing to this close attachment, the vaginal wall was torn during the enucleation and its lumen opened.

This rent in the vagina was first closed with interrupted sutures and the great gapping wound, from which the tumor was removed, was closed by drawing together the walls so as to obliterate the great dead spaces that would otherwise remain.

Subsequent History.—Wound healed by granulation.



Fig. 28 (Case VI).—Profile view of large fibro-lipoma of anterior vaginal wall.

Pathological Note.—The mass removed measures 11 cm. in length, 9 cm. in breadth, and 6 cm. in thickness. It is definitely encapsulated. The surface is smooth and of a reddish yellow color; surface vessels bein injected. The mass is irregularly lobular. The small area noted as being visible through the vulva is covered by adherent mucous membrane, measuring 2 cm. in diameter, which is hyperæmic and slightly ulcerated. The mass is solid, firm, somewhat elastic and of uniform consistency.

The cut surface is moist, glistening, not granular, but of a fibrous appearance. The general color is creamy white with numerous pearly white, glistening bands of tissue running irregularly through the mass. Nothing exudes upon pressure. There are some areas where the tumor does not appear so fibrous and where grossly there is a suggestion of myoxmatous tissue.

Microscopical Examination.—The sections of the tumor show it to be made up chiefly of fatty tissue, in which are scattered numerous irregular strands and areas of dense fibrous tissue. The tumor is a pure fibro-lipoma.

Case VII.—*Diagnosis. Hygroma.*

History.—Long-haired, black and white, English setter, five years old, a valuable animal and a pet, was brought to the clinic, March 10, 1905. The dog has always been well. About 5 months ago a swelling was noted over the right shoulder. This swelling has persisted up to the present time. No further history was obtainable.

Examination.—The patient is a very active dog, in excellent condition. Mucous membranes are of a good color. The coat is glossy and smooth. Upon palpation a small mass about the size and shape of a pigeon's egg is palpable in the right scapular region. This mass is circumscribed, firm, elastic, and smooth, shows a slight fluctuation, and is not adherent to skin or underlying structures.

Operation.—March 17, 1895. Morphia; ether. *Amputation of tumor.*

The mass, together with a large spindle-shaped portion of overlying, thick skin, was removed in one piece. The wound was closed without drainage, with interrupted fine silk sutures.

Subsequent history was uneventful.

Pathological Note.—The mass removed was found to be a cyst with a thin semi-translucent wall and of a bluish appearance. The contents of the cyst appear to be a clear fluid. The entire mass was placed in Zenker's solution for microscopical sections.

Microscopical Note.—The cyst wall is found to be composed of a dense layer of fibrous tissue, supporting, on its inner surface, a single layer of high, columnar epithelium. The inner surface is smooth and regular. The structure resembles that of a serous cyst.

Case VIII. *Diagnosis. Adenoma.*

History.—Long-haired, grayish yellow, Scotch-terrier dog, ten years old, a pet, was brought to the clinic, March 14, 1905. The dog has been apparently well until two years ago. At that time a small swelling, about the size of a pigeon's egg, was noticed in the left groin. At first, this swelling increased in size very slowly and remained at the original site. About six months ago the mass rapidly grew in size, gradually became more and more pendent as it increased in size, until it assumed its present proportions and position.

Examination shows an old, very active dog, seemingly in good health. Mucous membranes are of good color. Abundant *panniculus adiposus* is present. When the dog is standing upon all four feet, there is a large mass hanging by a pedicle, free from the abdominal wall at the side of the penis (Figs. 29, 30 and 31). The long pedicle is apparently composed of little more than skin and numerous large vessels, which can be palpated through it; one of these a large pulsating artery. One side of the pedicle forms a portion of the sheath of the penis. The mass just swings clear of the ground when the dog walks. The mass itself measures 12 cm. in length, by 10 cm. in breath, by 5 cm. in thickness, is covered by thin skin which is generally deeply pigmented, with the exception of several areas over the lower surface where there is an absence of pigment, suggesting healed abrasion and where there are several areas of recent abrasion. The mass is very soft, almost spongy on palpation. It is not definitely circumscribed, nor lobulated, though the surface is somewhat irregular. Some areas are definitely firmer than the rest of the mass. The entire tumor is very vascular.

The left inguinal glands are much enlarged and firm.

It was exceedingly difficult to make a clinical diagnosis. The case was brought in as one of hernia and had many points of resemblance to a hernia or a large varicocele in man though the scrotum was not involved. It resembled also a pendent lipoma such as is met with in man. The enlargement of the glands was accounted for by the ulcerated surface of the tumor. This tumor is exceedingly interesting because of the difficulty of diagnosis, because of its pendent nature and its rich blood supply and,

further, because it is our only instance of a tumor, other than a cyst, occurring in a male dog.



FIG. 29 (Case VIII).—Showing pendent nature of tumor with animal on all fours.

Operation.—March 17, 1905. Morphia; ether. *Amputation of tumor and pedicle, and removal of mass of enlarged inguinal glands.*



FIG. 30 (Case VIII).—Profile view of growth with patient in erect posture.

A long incision was made from the tip of the penis to the groin and carried along each side of the base of the pedicle. The large vessels were secured and the tissue containing the glands of the inguinal region, together with the tumor, was removed in one piece. The wound was closed with interrupted silk sutures, a new sheath of skin being made for the penis.

Subsequent History.—The wound broke down in part, healing slowly by granulation.

Pathological Note.—On section the tumor mass removed shows a dark red, much congested surface, which is moist, glistening, and granular. The whole tumor appears to be made up of very cellular tissue divided into small areas or lobules by a small amount of fibrous tissues; the picture resembling somewhat that of a thyroid. These lobules appear to be made up of smaller circular areas about the size of a pin head, which project from the surface upon pressure. Several small cysts are also to be noted, in two of which are small smooth bodies resembling papillomatous growths. There is a possibility of these being thrombi



FIG. 31 (Case VIII).—Front view. Growth suspended by penile sheath when animal is in this position.

in blood spaces or vessels. There are numerous large channels with thin smooth walls running through the mass. In the lower most dependent portion is a large island of fibrous tissue, firm, and of a pinkish color. In the subcutaneous tissue of the pedicle are found two sebaceous cysts each about the size of a large pea, resembling those found in man.

The inguinal glands are firm and present upon section a moist, deeply pigmented, congested center, with a paler periphery.

Microscopical examination shows the entire tumor to be made up of lobules, varying greatly in size. There is a very small amount of connective tissue around each lobule. The cells, making up the lobules, are chiefly large, granular, polygonal cells, with relatively clear, poorly staining nuclei. The stroma also appears to be very cellular. In many areas, the large cells form a solid lobule; in others, they surround alveoli; and in still other places alveoli are found, lined by cuboidal cells, and containing a peculiar substance, resembling cell detritus.

Histologically the enlarged lymphatic glands show merely a condition of endothelial hyperplasia.

The tumor was diagnosed as an adenoma, from its alveolar structure though it was impossible to say from what glandular tissue it had originated.

Discussion.

Tumors, and particularly carcinomata are of common occurrence in dogs. Gratia and Liénaux[1] report a series of six cases of carcinoma of the breast, which were used by them for inoculation experiments. E. Semmer,[2] of Dorpat, found among 3525 dogs, admitted to his clinic, 354 cases of tumor. Of this number about 8% were carcinomata. M'Fadyean[3] reports a series of 14 cases of tumor of the mammary glands of dogs. Fröhner's[4] figures for a period of eight years, ending with December, 1894, are exceedingly interesting. During this time, there were admitted to the veterinarian hospital and polyclinic in Berlin 60,471 dogs. Of this number 2871 had tumors, about one dog in every twenty. There were 1154 carcinomata; about 40% of all tumors, therefore, were of this nature.

Carcinomata of the skin and mammæ are the most common. These tumors generally appear late in the life of the dog. In my series of cases the age was obtainable in six cases; the youngest being five years and the oldest being sixteen years of age. Fröhner has never observed a carcinoma in a dog less than two years old. These tumors are most common in dogs between five and ten years of age, and occur more frequently in females than in males. Although carcinomata are the most common tumors of the breasts, nevertheless, fibromata, enchondromata, and sarcomata are not infrequently met with.

It seems to be a common opinion among veterinarians that when a tumor of the mamma has a bony structure, such as several of our cases exemplify, it is undergoing retrogressive changes or a process of self-healing. This view does not seem to me to be the correct one, in the light of my limited number of cases. The adenomatous portions of the tumors appear to be the portion that metastasizes.

I have been unable to find, in the literature at my command, any tumor corresponding to Case VIII, except one reported by Kitt.[5] The one described by him occupied a similar position, was the same shape, and presented a similar gross appearance before removal. However, from his description after removal, the tumors do not resemble one another. Kitt's tumor was an adenoma sebaceum (*Talgdrüsenadenom*).

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CASES OF HERNIA IN DOGS.

By F. C. Beall.

Case I.—*Large irreducible, right, inguinal hernia: enterocele; cystocele.*

The patient, an old fox-terrier bitch, was admitted November 5, 1904. The only history obtainable from her owner, beyond the fact of several pregnancies, states that for six months there has been a noticeable tumor in the lower abdominal region. This



Fig. 32 (Case I).—Large right inguinal hernia containing intestines and greatly distended bladder.

has been progressively enlarging. For the last two months the dog has been losing in weight and strength. Latterly she has been vomiting almost every day. There has been constant dribbling of urine.

Examination shows an old, seemingly well bred, though poorly nourished, animal with pale mucous membranes.

Hanging from the left half of the abdomen is a large, soft tumor (Figs. 32 and 33), covered by normal, freely movable skin, which has a faintly bluish tinge. Coursing irregularly over its surface are ridges made by several greatly dilated subcutaneous veins. The tumor is generally smooth and rounded except near its base on the median surface. Here, the two lowest mammary glands have been drawn out onto the tumor by the stretching of the skin, and, in consequence, an area about the size of the hand is roughly and loosely folded. On the posterior wall of the tumor, just below the symphisis pubis, as the patient stands, is a purplish ecchymotic area. Palpation of the contents of the tumor show that it is composed of two distinct parts. One, a more or less pear shaped mass, constitutes its main bulk and is every-

where, except just at its base, in contact with the overlying skin, though not attached at any point. This portion of the tumor is distinctly pedunculated, rather firm and elastic, giving the impression of a very thick walled cyst without distinct fluctuation. Around the base of this harder mass, especially on the median side, can be made out a softer, irregular, "wormy" mass that does not seem to be connected with the firmer portion of the tumor. It can be traced across the median line to the right inguinal ring which is easily made out. In this soft mass at the base of the tumor, peristaltic movements were discernible while the animal was being cleaned up for operation. The tumor could not be reduced by taxis even under the anæsthetic.

Operation.—November 11, 1904. Morphia; ether. *Herniotomy.*

A long incision was made through the skin on the mesial side of the neck of the tumor. The sac was exposed and liberated as well as possible, but owing to its large size was very awkward to handle nor could any of its contents be reduced until it had been



Fig. 33 (Case I).—Lateral view of hernia sac.

opened and the inguinal ring identified and incised in the line of the external oblique fibres.

In addition to the round ligament, which in the dog normally passes through the inguinal ring with a process of peritoneum, the sac contained about 200 cc. of a pale straw colored fluid, a free, irregularly shaped blood-clot, the size of a walnut, several loops of small intestine, one of which was a dark bluish color—apparently almost strangulated—and a very large distended bladder, measuring 12 by 6 by 8 cm. (The length of the bladder, normally, in a dog of this size is about 3 cm.) The surface over the fundus of the bladder was congested, granular and covered in part with a fibrinous deposit, evidencing an old hæmorrhagic peritonitis and doubtless the source of the free blood-clot found in the sac. Some difficulty was experienced in reducing these structures; this was particularly true of the bladder and a considerable enlargement of the ring was necessary before it could be replaced in the abdomen. The sac, which was very thin and tore in several places despite the greatest care, was then freed; its neck was ligated and the fundus cut away. The abdominal wound was closed in layers, the internal oblique fibers having been brought down to Poupart's ligament and secured by imbricating as were also the edges of the external oblique aponeurosis. The operative procedure differed but little from that advocated for the corresponding lesion in man. The only anatomical differences lay in the presence of a large venous radicle from the epigastric which passed through the external ring.

Post-operative.—Though the animal stood the operation well and no serious complications were anticipated, she was found dead the following morning.

Autopsy.—The examination revealed the following conditions: The whole mucosa of the stomach, except just around the pylorus, was thickly studded with deep ulcers, some of them extending through all but the serous coat of the stomach wall. The ulcers were sharply outlined and had elevated hæmorrhagic edges showing that they could not have been due to post-mortem digestion. The right kidney was completely atrophied, its substance being



Fig. 33 (Case II).—Large left and small right inguinal herniæ.

represented by a dense fibrous tissue only 4 mm. in thickness. The ureter in this side, though patent throughout, was only about one-third the size of the one on the left. The bladder was very large—10 cm. in its longest axis—and presented the appearances described with the operation. The walls were about ½ cm. in thickness. The mucous membrane was swollen, rough and of a dark red, almost black color at the fundus. The other organs were practically normal.

Anatomical Diagnosis.—Recent operative wound. Chronic, round ulcers of the stomach. Obstructive hypertrophy with congestive inflammation of the bladder. Atrophy of right kidney and ureter.

Case II.—*Bilateral inguinal hernia.*

The patient, a little, old, shaggy-haired bitch, of Skye-terrier type, was admitted January 13, 1905. The history obtained from her master is as follows: The dog is eight years old. She has twice been pregnant, having had only one pup at the first, and two at the second occasion. She is a very active dog and her owner thinks the ruptures are due to "jumping after cats."

against high palings. Two years ago and not until two years after the second pregnancy, a tumor was first noticed in the left inguinal region. When first seen it was small and reducible. It has gradually increased in size until now it is about as large as a closed fist (Fig. 33). A second tumor was noticed on the right side about two months ago. It is now about the size of an egg.

The larger tumor, on the left side, is not reducible; the one on the right usually disappears of itself when the dog is relaxed and placed upon her back.

Operation.—January 13, 1905. *Radical cure of left inguinal hernia.*

The sac was cut down upon by an oblique incision, carried upward and outward from the external ring in the line of the external oblique fibres. The sac was dissected out, opened, its contents —in this case small intestine only—replaced in the abdominal cavity. The sac was ligated at the external ring and excised. The wound was closed in layers with fine silk interrupted sutures, imbricating the external and internal oblique muscles as in Case I.

Recovery was uneventful. The wound healed per primam.

Operation 2d.—February 10, 1905. *Radical cure of right inguinal hernia.*

An operation similar to that above described, was performed upon the right side, where the small hernia had, in the interim, increased in size almost to that of the original large left hernia. The recovery was rapid and complete with primary union.

Case III.—*Small right inguinal hernia.*

The patient, a fine large Gordon-setter bitch (No. V, of Mr. Ortschild's series), was operated upon by Mr. Ortschild and myself, February 15, 1905, for the removal of a large malignant tumor of the right inguinal breast. In the fatty tissue under the breast a small hernial sac, containing the prolapsed round ligament and its meso-ligamentum, was unexpectedly found. The hernia was treated as in the other instances.

Discussion.

Hernia, as is well known, is frequently met with in the dog. The most common form, perhaps, is the mid-ventral, either epigastric or umbilical, of which we have seen several instances. These ruptures occur in both sexes with about equal frequency and, according to our experience, are usually small and not productive of symptoms. They are usually congenital. Inguinal hernia, on the other hand, aside from the very rare congenital form, is very much more common in the female and, as in the cases cited above, may reach a seriously incapacitating size. The smaller inguinal hernias, such as the last case illustrates, are probably not at all uncommon in bitches and we have heretofore in the clinic doubtless overlooked them many times. What were at first considered to be merely hypertrophied inguinal mammæ, have, on several occasions, been found to be normal breasts whose prominence was due to an underlying rupture. In one of Mr. Ortschild's cases a piece of tumor had been implanted in one of these supposedly enlarged breasts which increased further in size and led us to believe that the tumor itself was enlarging. The dog became emaciated and one morning was unexpectedly found dead. The autopsy disclosed a hernia containing a strangulated loop of small intestine.

All of the cases but one, that I have been able to find in the veterinarian literature, have occurred in the female. This was a case of Parascandale's.[13] The greater frequency of this form of hernia in the female is doubtless to be explained on anatomical grounds. The broad ligaments of the dog's bicornuate uterus are attached to the horns just as the mesentery is to the intestine, forming the mesometria. The round ligaments arise as processes from the broad ligaments at about their middle and run backwards to the inguinal canals (the uterus of the dog, it is to be remembered, is for the most part an abdominal organ) carrying with them processes from the broad ligaments. Each round ligament, as it passes through the inguinal canal, is practically free, being attached only loosely to the dorsal wall of the canal by folds of peritoneum which are continuous with those of the broad ligament. The canal is lined by an extension of peritoneum (analogous to the Canal of Nuck) which passes about 2 cm.—in a medium sized dog—beyond the external abdominal ring. There exists normally, therefore, a peritoneal diverticulum which traverses the abdominal parietes. With the dog on its four feet this sac looks backward, inward, and slightly upward and the pressure of the abdominal contents on its upper wall probably serves to keep it entirely closed. During pregnancy, however, the round ligament is put on a stretch by the enlarged uterus, and this seemingly tends to loosen and weaken the surrounding structures and to enlarge the whole canal. After pregnancy the relaxed tissues would allow the small peritoneal sac to sag and point downward, instead of upward, so that with an enlarged opening the prolapse of abdominal viscera would be comparatively easy. That the frequency of inguinal hernia in the female dog is due, in great part at least, to the weakening effects of pregnancy on the abdominal wall, is shown by the fact that this form of hernia is almost unknown in the male dog. And this, notwithstanding the fact that the tunica vaginalis of the testicle retains its peritoneal connection through the inguinal ring and does not become obliterated as in man.[14]

[13] Un caso di ernia doppia in un cane. Mod. zoöiatro, Torino, 1900, XI (221-6).

[14] The persistence of these peritoneal canals is very commonly regarded as a favoring cause of inguinal hernia (of the so-called congenital variety) in man and his erect posture may suffice to make this the more probable. Bland Sutton, however (Transactions of the Pathological Society. London, Vol. XXXIX, 1888), has called attention to the fact that these peritoneal processes remain patent in the monkey and yet inguinal hernia is a rare malady in these animals. He has made a report upon a single instance of the condition.

He says, "Some surgeons are of the opinion that a patent funicular pouch is to be regarded as predisposing to the occurrence of a hernia." * * It is, however, a remarkable fact that, among mammals, obliteration of this process above the testis is altogether exceptional, indeed, in the majority this process not only remains open but freely communicates with the peritoneal cavity. The only exceptions which have come under my notice are the chimpanzee and the gorilla. Professor Owen has found the process obliterated in a chimpanzee. In three specimens of this mammal dissected by me the process was patent. * * * * * Up to the present time I have examined post mortem more than

The viscera, most often found in these canine hernias, are the round and broad ligaments of the uterus, the uterus itself (sometimes even the pregnant uterus), the small intestine, and the omentum. Our first case is of interest in that the sac contained the entire bladder which had become greatly distended and hypertrophied. I have been unable to find any other case of cystocele reported as occurring in the dog although the possibility of its occurrence is mentioned.

800 monkeys, including examples of all the chief species, excepting the gorilla. In every male, the funicular process was unobliterated and communicated freely with the peritoneal cavity. There was no separation of a piece to form a tunica vaginalis. * * * * Theoretically, if an unobliterated funicular pouch predisposes to hernia, this accident should occur in monkeys frequently. So far I have only seen three cases. In each instance they were of the variety known as congenital, the contents completely surrounding the testis."

The malady in the canine does not seem to be commonly attacked on modern surgical principles by veterinary surgeons. A series of twelve cases has been reported by Hobday from the Royal Veterinary College of London.[15]

In his Operationslehre für Tierärzte, Hering states that inguinal hernias are most commonly met with in stallions and boars, rarely in oxen, sheep, and dogs, and very exceptionally after castration. He describes, in addition to the more common forms which we have met with, several other varieties of hernia that occur in animals and which are anatomically similar to those met with in man.

[15] Hobday, Operative Treatment for Hernia in the Dog. Veterinarian, London, 1896, LXIX, 195-200. Cf. also, Einige Beobachtungen über Hernien. Wchnschr. f. Tierh. u. Viehzucht, München, 1897, LXI, 217, 225, 229. Duscourneau, Hernie inguinale irréductible chez la chienne. Bull. Soc. Centr. de Méd. Vét., Paris, 1901.

CORRESPONDENCE.

Boston, Feb. 16, 1905.

The Editor of the Johns Hopkins Bulletin, Baltimore, Md.

Dear Sir: The Johns Hopkins Bulletin of August, 1904, contains an interesting article by Dr. Walter R. Steiner, of some early autopsies in the United States, in which he mentions five cases included in the years 1639-61, as probably the earliest on record. In the narrative of Samuel de Champlain, are given accounts of still earlier autopsies, probably the first in North America, performed in the spring of 1605, at the St. Croix Island, and in the winter of 1605-06 at Port Royal.

The original and official narrative[1] is found only in a few great libraries of the world. A complete copy of the original was edited by Abbé Laverdiére under the patronage of Laval University of Quebec, in 1870. In 1878, this copy was translated by Otis for the Prince Society of Boston. A portion of this narrative, including that which deals with the autopsies, was also translated by W. T. Ganong, and published in the Champlain number of "Acadiensis," July, 1904.

The following are extracts from the translation of Otis:

VOL. II, CHAPTER VI.—Pp. 40 to 54.[2]

"Of the mal de terre, a very desperate malady.—How the Savages, men and women spend their time in winter. And all that occurred at the settlement while we were passing the winter.

"When we arrived at the Island of St. Croix, each one had finished his place of abode. Winter came upon us sooner than we expected, and prevented us from doing many things which we had proposed. Nevertheless, Sieur de Monts did not fail to have some gardens made on the island. Many began to clear up the ground, each his own. I also did so with mine, which was very large, where I planted a quantity of seeds, as also did the others who had any, and they came up very well. But since the island was all sandy, everything dried up almost as soon as the sun shone upon it, and we had no water for irrigation, except from the rain, which was infrequent.

"Sieur de Monts caused also clearings to be made on the mainland for making gardens, and at the falls three leagues from our settlement he had work done and some wheat sown which came up very well and ripened. Around our habitation there is at low tide a large number of shell-fish, such as cockles, mussels, sea-urchins and sea-nails, which were very acceptable to all.

"The snows began on the sixth of October. On the third of December we saw ice pass which came from some frozen river. The cold was sharp, more severe than in France, and of much longer duration; and it scarcely rained at all the entire winter. I suppose this is owing to the north and northwest wind passing over high mountains always covered with snow, which was from three to four feet deep up to the end of the month of April; lasting much longer, I suppose, than it would if the country were cultivated.

"During the winter,[3] many of our company were attacked by a certain malady called the mal de la terre; otherwise scurvy, as I have since heard from learned men. There were produced in the mouths of those who had it great pieces of superfluous and drivelling flesh (causing extensive putrefaction), which got the upper hand to such an extent that scarcely anything but liquid could be taken. Their teeth became very loose, and could be pulled out with the fingers without its causing them pain. The superfluous flesh was

[1] Champlain's Voyages, published with his maps and sketches in Paris, 1613.

[2] Pub's. Prince Society, Boston, Vol. XII. Champlain's Voyages, Vol. II, 1604-1610.

[3] 1604-5.

often cut out, which caused them to eject much blood through the mouth. Afterwards a violent pain seized their arms and legs, which remained swollen and very hard, all spotted as if with flea-bites; and they could not walk on account of the contraction of the muscles so that they were almost without strength and suffered intolerable pains. They experienced pain also in the loins, stomach, and bowels; had a very bad cough and short breath. In a word, they were in such a condition that the majority of them could not rise nor move and could not even be raised up on their feet without falling down in a swoon. So that out of seventy-nine, who composed our party, thirty-five died, and more than twenty were on the point of death. The majority of those who remained well also complained of slight pains and short breath. We were unable to find any remedy for these maladies. A post-mortem examination was made of several to investigate the cause of their malady.

"In the case of many, the interior parts were found mortified, such as the lungs, which were so changed that no natural fluid could be perceived in them. The spleen was serous and swollen. The liver was legueux[1] and spotted without its natural color. The vena cava, superior and inferior, was filled with thick coagulated and black blood. The gall was tainted. Nevertheless, many arteries, in the middle as well as lower bowels, were found in very good condition. In the case of some, incisions with a razor were made on the thigh where they had purple spots, whence there issued a very black clotted blood. This is what was observed on the bodies of those infected with this malady. Our surgeons could not help suffering themselves in the same manner as the rest. Those who continued sick were healed by spring, which commences in this country in May. That led us to believe that the change of season restored their health, rather than the remedies prescribed.

"During this winter all our liquors froze, except the Spanish wine. Cider was dispensed by the pound, etc."

He does not mention the names of the surgeons who performed the autopsies, but in Chapter XI, p. 98, the chapter which treats of the winter 1605-6, spent at Port Royal,—now Annapolis, Nova Scotia,—he mentions several post-mortem examinations, as having been performed by desChamps. He states:

"After making this observation, we returned to our settlement, where we found some of our company sick with the mal de la terre, but not so seriously as at the Island of St. Croix; although, out of our number of forty-five, twelve died, including the miner, and five were sick, who recovered the following spring. Our surgeon, named desChamps, from Honfleur, skilled in his profession, opened some of the bodies to see if he might be more successful in discovering the cause of the maladies than had been our surgeons the year before. He found the parts of the body affected in the same manner as those opened at the Island of St. Croix, but could discover no means of curing them, any more than the other surgeons.

"On the 20th of December it began to snow, and some ice passed along before our settlement, etc."

JOHN W. LEWIS.

[1] Woody.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

March 6, 1905.

Résumé of History of Blood Platelets. DR. OSLER.

The Symposium on the Blood Platelets was opened by Dr. Osler, who gave a résumé of the history of the subject. The blood platelets had, he said, attracted a great deal of attention between 1857 and 1867 after the appearance of Schulze's original article in the *Archiv für mikroskopische Anatomie;* and their clinical significance was promptly studied by Ries, who wrote the first paper on this subject. In 1873 Osler, working in London, noticed peculiar bodies in the blood of subcutaneous and mesenteric vessels of white rats; and these he found to be the individual elements of Schulze's granule masses or agglutinated plates. Zimmerman had seen the same things previously and had called them elementary corpuscles. When watched on a warm stage Dr. Osler and others noticed marked changes rapidly taking place in the platelets which became elongated and diamond-shaped and finally appeared as threads. It was suggested that they might be parasites; but in 1878 Hayem, in a large work on the subject, called them hæmatoblasts, testifying to his belief that the platelets played a rôle in the genesis of red-blood corpuscles. Bizzozero then showed the platelets to be individual elements and studied their relation to the red-blood corpuscles working along the lines of Ranvièr's previous suggestions. Next came the demonstration of the importance of platelets to blood coagulation —the work of Eberth and Schimmelbusch; which was followed by Osler's observation that white thrombi were made up largely of platelets. Modern study of the question has been concerned with determining whether the platelets were independent blood elements, whether they were precursors of the red-blood corpuscles, or whether they were artefacts due to cellular disintegration. The platelets have been usually overlooked in routine examinations; and their association with disease has not been carefully studied—though their great increase in the wasting diseases was noted by Osler long ago.

Histology of the Blood Platelets.—Professor Kemp, of Champaign, Ill., said that in the relatively few years that blood platelets had been known an enormous literature had sprung up on the subject.

The platelets were best studied, he said, after immediate

fixation; or by working in a low temperature and with cold glassware when the changes in the platelets were slow and could be watched. At the end of some minutes (when studied at 40° F.) they became granular, irregular in form, gradually lost their individuality, fused into a mass and finally broke down. Pari passu with these changes came the clotting of the blood, the fibrin being deposited thickly about the blood platelets but independent of them—though the possibility of coagulation with intact platelets had never been proven. A smear of blood passed rapidly into a salt solution (to wash off the corpuscles) and then put into 1% osmic acid solution gave a beautiful fixation specimen of platelets. There has been a good deal of discussion as to whether oval, discoid platelets were biconcave or not and the change in shape due to the change in containing fluid. They probably do not contain hæmoglobin, though Professor Kemp said that he had seen platelets, during some observations at a high altitude, which seemed to be exceptions to this statement. Their function is still a debated question though it seems probable that they are hæmatoblastic. The figures given by Arnold, which the author thought proved the platelets to be degenerated red cells, probably represented artefacts. Löwit thought the platelets to be precipitated globulins and not true blood elements; but their observation by Osler within the blood-vessels and later by Bizzozero's son in the frog's mesentery and the bat's wing seem to prove them independent elements. They are best counted by the indirect method—determining first the red blood count and then the ratio of platelets to erythrocytes. Professor Kemp found experimentally that if blood from an artery be defibrinated and injected back into a vein, the platelets (after sufficient repetition of defibrination and injection) disappeared and the blood refused to clot.

Relation to Disease.—Dr. J. H. Pratt, of Boston, referred first to the great confusion existing in the literature as to the platelets and said that there were marked differences between the Arnold bodies, which were artefacts, and true platelets. A good preparation of them could, he said, be prepared by fixing the smear in a solution of sodium metaphosphate in sodium chloride. Stained by certain methods chromatin may be shown in them and a pseudo-amœboid movement has been observed. In health the number of platelets varies greatly but they average about 300,000. Dr. Pratt reported a series of diseased conditions with the plate count in each. The lowest count (7000) was made in a case of purpura hæmorrhagica. The platelets were never absent but were greatly reduced in number in lymphocytic leucæmia (series of 8 cases, count varying from 10,000-94,000) and in pernicious anæmia (series of 10 cases). In secondary anæmias they may be increased—a point which may be of diagnostic value in distinguishing from primary anæmia. An increase in platelets was found in myelogenous leucæmia (count varying from 500,000 to 1,498,000), in chlorosis, in erythrocytosis, and in *severe* hemorrhage. Dr. Pratt thought the evidence was conclusive for regarding platelets as third corpuscles.

Dr. Emerson said that he had often seen pseudopods extended from platelets but never any real amœboid motion with progression. The endoglobular degenerations of Maragliano had been shown to have a distinct existence; and it was possible that the platelets might represent extruded "innere Körper" or might be due to the disappearance of the red-blood cell from about the "innere Körper." Dr. Osler said that the changes seen in the platelets were similar to the mechanical changes occurring in red-blood corpuscles, and were not truly amœboid. The great number of platelets in embryos and in wasting diseases had never been explained. Dr. Boggs referred to recent work done in Germany in reference to the relation of platelets to coagulation. It was found that if fibrinogen be treated with a mass of pure blood platelets coagulation occurred rapidly, but took place much more slowly if leucocytes were used instead of platelets.

March 20, 1905.

The Scope and Problems of Surgical Physiology. Dr. George W. Crile, of Cleveland, Ohio.

Surgery in its early days had been, Dr. Crile said, anatomical and empirical; but it had been wholly transformed by the origin and development of pathology and bacteriology. Physiology in its surgical relations was now, however, coming to the fore as it was more and more realized how often surgical treatment rested on an understanding of surgical physiology. A stoppage of respiration, for instance, due to reflex inhibition, was a very different phenomenon from a similar stoppage due to obstruction, and demanded, therefore, a different sort of surgical interference. Respiratory arrest could be caused by strong traction on the tongue and a knowledge of this physiological fact might relieve anæsthetizers of embarrassment who, in their efforts to produce respiration might, in their ignorance of physiology, be defeating their own purpose. The reflex effects of peritoneal manipulations were often overlooked and the reflex expulsion of intestines, through an abdominal wound, was often blamed on the anæsthetist when it was due really to peritoneal irritation. The surgical physiology of the circulation was of the utmost importance and yet it was very incompletely understood. Often life itself and more often still immediate operative results depended on the proper care of the circulation. Independent of anæsthesia the mere handling of tissues might impair or even throw out of function completely the vasomotor centers; and a proper knowledge of the facts would make efforts to afford these centers efficient support more intelligent. The result of an operation is equal to the sum of the insults caused the tissues; and blocking of certain of these insults, by intra-neural cocainization has minimized or even abolished shock after even such serious procedures as double thigh amputations. The mere opening of an appendicial abscess under cocaine with an extensive curative operation later when the procedure could be carried on within physiological limits was a good example of the safety of operative physiologic progression. Many of the facts of compensation by one organ for another were quite

unknown and yet a knowledge of them would be most important for surgical treatment. The nature of protoplasmic response to changed environment, determination of minimum circulatory requirements for each organ, discovery of practical methods for helping organs over a surgical crisis, the whole question of physiology of the lymphatics, of the surgery of thrombosis and embolism, of shock—here were problems almost untouched. The intricate problems of brain localization in human beings were still to be developed. And might it not be possible by cocainization to effect functional detachment of the medulla to protect it from injurious surgical stimuli? There had been hitherto a surgical fear of the heart; yet perhaps in the future operations on the valves might not be impossible. Our knowledge of the pulmonary circulation was infantile; surgery of the stomach had but just been opened and the supra-renals, thyroid, and pituitary body had been almost untouched.

Dr. Howell said that thirty years ago, when Ludwig and Virchow were doing their work, the association between medicine and physiology had been intimate. With the prominence of pathology and bacteriology, however, the two had been somewhat divorced; but it was gratifying to see surgeons again coming back to physiology. The problems in surgical physiology were, however, very difficult ones and were not to be thought of as simple; for they depended, ultimately, on physiological fundamentals, and these were difficult for even specially trained physiologists to master.

Partial Occlusion of the Aorta. Dr. Halsted.

Dr. Halsted reported some experimental work done by himself and Dr. Sowers on this subject. Ligation of the aorta had been tried fourteen times in human beings and had always been fatal. The early experimental work on the subject had been done by Pirogoff, but, on account of his septic technique, it had not been successful. Dr. Halsted used for ligation a metal band which could be gradually tightened until obliteration was complete. Contrary to what might be expected no gangrene of the lower extremities occurred; but Stenson's phenomenon (paralysis of the extremities due to anæmia of the cord) was present. As a rule in time the circulation became completely shut off; but just before this occurred an equilibrium was apparently established between the blood above and that below the ligature, and there were evidences that in some cases the pulse reappeared below after having disappeared. No evidence of clot formation was seen nor was there any endothelial proliferation in the arterial wall, which was normal except for atrophy. In certain cases the metal band cut through and lay within the vessel; and in one or two cases a semilunar diaphragm formed within the aorta. Contrary to the experimental findings of Lister no endothelial proliferation took place.

The Blood Pressure in Different Parts of the Arterial Tree. Dr. Dawson.

Dr. Dawson reported a study of this subject which was undertaken to determine the changes undergone by the systolic, the diastolic, and the mean pressures in passing from the heart to the periphery. The aortic-cephalic, the aortic-brachial, and the aortic-femoral systems of the dog were studied—a cannula being introduced into the aorta and then into the successive parts of each of these systems moving toward the periphery. The various blood pressures were read in each of these situations. An unexplained initial rise occurred near the heart—the pressure measured at a point nearest the heart being slightly lower than at a point a little distal to that.

Heart Block in Mammals. Dr. Erlanger.

Dr. Erlanger reported experimental work done in connection with heart block in mammals. Complete heart block may be said to be present when the auricle and ventricle are beating with independent rhythms, and though a well-known phenomenon in cold-blooded animals, this had never before been produced in the mammalia. Dr. Erlanger's experimental work started with the study of a case of Stokes-Adams disease in the Johns Hopkins Hospital. It was found, by careful pulse tracings, that the auricle and ventricle in this patient beat with different rhythms. The administration of atropine had the usual effect on the auricular beat; but the ventricular beat did not change, the ventricle thus shown to be uncontrolled by the vagus. The accelerators were, however, shown to influence both auricle and ventricle. During the attacks the ventricles stopped but the auricles continued to beat. All these phenomena led Dr. Erlanger to the conclusion that Stokes-Adams disease was ultimately heart block. He then tried to produce this condition in dogs, and was finally able to accomplish it by inserting a specially devised hook-clamp between the auricle and ventricle and compressing with it the auriculo-ventricular muscle bundle of His. The study of the case and the further experimental work on dogs showed conclusively that every case of Stokes-Adams disease (the rhythm in the neck vessels different from the rhythm at the heart, being one of the features described by Stokes) was in reality an instance of heart block; and a study of all the cases in the literature which have been well observed and by adequate methods confirmed this idea. All the symptoms, Dr. Erlanger said, could be explained by a lesion of the auriculo-ventricular bundle of His, and there seemed to be neither need nor warrant for calling in the cardiac nerve centers to explain the condition.

NOTES ON NEW BOOKS.

A Treatise on Bright's Disease and Diabetes with Especial Reference to Pathology and Therapeutics.—By James Tyson, M. D., Professor of Medicine in the University of Pennsylvania. Second Edition, Illustrated. Including a Section on the Ocular Changes in Bright's Disease and in Diabetes, by George E. de Schweinitz, M. D., Professor of Ophthalmology in the University of Pennsylvania. (*Philadelphia: P. Blakiston's Son & Co., 1012 Walnut Street, 1904.*)

Dr. Tyson's special interest and long experience in the observation and treatment of Bright's disease and diabetes should cause the profession to welcome with pleasure this second edition. The

first edition appeared in 1881 and had for many years been out of print. In the meantime many contributions to our knowledge of these only too prevalent diseases had been made, and the present edition brings the work well up to date. A considerable part of the original edition has been re-written, and valuable additions have been made. The volume contains a number of useful illustrations.

The author introduces the subject of Bright's disease with a valuable chapter on the gross and microscopic anatomy of the kidney. Although Dr. Tyson recognizes the difficulty in diagnosticating with any great degree of accuracy the various types of Bright's disease, he prefers to adopt the following clinical classification: I. Acute Bright's disease, including (1) acute parenchymatous; (2) acute diffuse; and (3) interstitial nephritis. II. Chronic Bright's disease, including (1) chronic diffuse nephritis represented by the large white kidney, and its second or indurated stage the small white kidney; (2) chronic interstitial nephritis (primary contracted kidney); (3) arterio-sclerotic induration. III. Amyloid degeneration of the kidney. IV. Cyanotic induration (passive congestion). V. Suppurative nephritis including tuberculosis of the kidney. It may be well to emphasize that authorities are now beginning to recognize an acute interstitial nephritis, to which the author devotes an interesting chapter.

Dr. Tyson fails to throw any light on the much discussed question as to the essential cause of the symptoms of uræmia. The subject is dismissed with the statement that they are "ascribed to the accumulation of excrementitious substances in the blood." He thinks that we have stuck too rigidly to the view that meats are injurious in nephritis and, with von Noorden, advocates the giving daily of moderate quantities of meat and an egg at breakfast in cases of chronic nephritis.

The chapters on diabetes mellitus give a concise and clear picture of the disease. We regret to observe that Dr. Tyson does not think that much importance is to be placed on the occurrence of hyaline degeneration of the islands of Langerhans in the pancreas from an etiological standpoint. We are inclined to think that more significance should be assigned to this interesting observation of Opie's, especially in view of Prof. Otto Cohnheim's researches on carbohydrate metabolism which appeared in 1903 and which we fail to find any reference to in the volume. Cohnheim found that the expressed juice of the pancreas had no action when added to a solution of glucose. The same result followed when muscle juice was added to glucose. When the two juices were mixed and then added to glucose there was a rapid and complete conversion of the sugar into alcohol and carbonic acid. The view advanced was that the pancreas and muscles produced enzymes or pro-enzymes, each of which was necessary to the other to effect carbohydrate combustion. It is probable that the islands of Langerhans have to do with the production of the internal secretion of the pancreas and consequently with the glycolytic ferment. If they be diseased this ferment is wanting and the sugar is not burnt up in the muscles. It accumulates in the blood and is excreted in the urine, giving rise to the symptoms of diabetes.

There is a very good chapter on diabetes insipidus.

The value of the volume is enhanced by excellent chapters on the ocular manifestations of Bright's disease and diabetes by Dr. G. E. de Schweinitz, with several colored illustrations of retinal changes.

Diet in Health and Disease. By JULIUS FRIEDENWALD, M. D., Clinical Professor of Diseases of the Stomach in the College of Physicians and Surgeons, Baltimore, and JOHN RUHRÄH, M. D., Clinical Professor of Diseases of Children in the same College. (*Philadelphia, New York, London: W. B. Saunders and Company, 1905.*)

This volume of 689 pages will undoubtedly prove of great practical value to students, hospital internes, nurses and practitioners, particularly the latter. As would be expected, the authors first give an account of the physiology of the food-stuffs and of the processes in normal metabolism.

Chapters are devoted to the various classes of foods—animal and vegetable—also to fruits, nuts, etc. Atwater's views regarding the effect of alcohol as a food and stimulant are quoted at length and apparently accepted. Food adulterations and diseases resulting from food poisoning are dealt with in a concise and interesting manner.

Considerable space is devoted to infant feeding and milk-modification. The methods and formulas for changing the composition of the milk according to the age of the infant are given in detail. Rectal alimentation is thoroughly treated.

The diet in the various infectious diseases is duly considered. Special attention is given to the dietetic treatment of gastric and intestinal disorders, and of certain diseases in which diet is a primary factor, such as diabetes mellitus, gout, obesity and nephritis.

Army and navy rations, prison and hospital dietaries are described. A particularly valuable section is devoted to sick-room recipes. For those interested in metabolism experiments there is a very important chapter in the chemical composition of American food materials, giving the percentage of proteids, fats, carbohydrates, water, ash, etc., and also their caloric value.

It is only too often the case that books are written and published, without their being any real need for them. The authors have done the profession a real service, however, by placing before it a thorough and practical treatise on the dietetic management of disease. The general make-up of the book is attractive and it is made especially serviceable by an unusually good index. The general practitioner will find the volume of inestimable value in the treatment of his patients if he gives to the dietetic management of disease the importance it deserves.

Practical Dietetics. By A. L. BENEDICT, A. M., M. D. Gastro-Enterological Association, etc. (*Chicago: G. P. Engelhard & Company, 1904.*)

The appearance recently of text-books on dietetics is timely. Sufficient importance has not been attached by physicians to the regulation of the diet in health and in diseased conditions. A worthy book on this subject must, therefore, be welcome to the profession.

This comparatively small volume of 383 pages describes the principles which underlie the regulation of the diet in health and disease. The chemical constitution of the body tissues and of the various types of foods is first discussed. The writer then proceeds to outline the diet for the various stages of the period of growth and in the various individual diseases. A chapter is devoted to organotherapy which, with two or three brilliant exceptions, has up to the present proved very disappointing as a means of coping with disease. Altogether, the volume is a useful addition to the limited number of works devoted to dietetics.

Modern Microscopy. A handbook for Beginners and Students. Combining: I. The Microscope and Instructions for its Use. By M. I. CROSS. II. Microscopic Objects: How Prepared and Mounted. By MARTIN J. COLE, Lecturer in Histology at Cooke's School of Anatomy. Third edition, entirely revised and enlarged. To which is added, III. Microtomes: Their Choice and Use. (*Chicago: W. T. Keener & Co., 90 Wabash Avenue, 1903.*)

The title of this volume of 292 pages indicates fairly well its scope. This edition brings the knowledge of the microscope and its accessories well up to the date of its issue. The book is intended to instruct the beginner in the care and use of the various parts of the microscope, consequently advanced work such as micro-photography is not included.

The section on the preparation and mounting of microscopic objects is concise and practical and serves well the purpose intended. The methods of hardening and staining tissues are described, but not sufficiently in detail to help the advanced student. The various microtomes and the method of using them are described in detail. The little volume is well illustrated. We know of no book that will be of greater aid to the student in acquiring a knowledge of the microscope and the method of using it.

Practical Pediatrics. A manual of the Medical and Surgical Diseases of Infancy and Childhood. By E. GRAETZNER, Editor of the Centralblatt für Kinderheilkunde and the Excerpta medica. Authorized Translations with numerous additions and notes, by Herman B. Sheffield, M. D., Instructor in Diseases of Children, and attending Pediatrist (O. P. D.), New York Post Graduate Medical School and Hospital. Flexible Cloth. (*Philadelphia: F. A. Davis Co., 1905.*)

To condense into a volume of the size of the present one a practical treatise on the medical and surgical diseases of children is a difficult undertaking, and while this book is as satisfactory as condensations of medical text-books usually are, it is necessarily fragmentary and of no special value to those seeking a thorough knowledge of pediatrics.

It is impossible to treat fairly such subjects as infant-feeding, indigestion, diarrhœa, typhoid fever, diseases of the respiratory tract and the various orthopædic subjects attempted in the space allotted to them.

The value of the book is much enhanced by the translator whose notes present in a number of instances, generally accepted views, which differ somewhat from the author's. Particularly is this noticeable in the discussion of intubation. He has added, too, a detailed description of the operation of Lorenz for congenital hip dislocation. The chapters on physical diagnosis and contagious and infectious diseases, with the exceptions noted, will be found very satisfactory.

Part II of the volume is given up to materia medica and therapeutics, including a discussion of hydrotherapy, saline infusions, electricity, and a short description of most of the drug preparations useful in the diseases of children.

On the whole, the book seems better suited for a rapid review of the subject than for reference purposes of the practitioner.

Post-mortem Pathology. A manual of post-mortem examinations and the interpretations to be drawn therefrom. A Practical Treatise for Students and Practitioners. By HENRY W. CATTELL, A. M., M. D. Second revised and enlarged edition (*J. B. Lippincott Co., Phila., 1905.*)

The author announces in the preface to the first edition that "This book has been written for those who ought to make autopsies but do not." One would think, however, from reading the book that it was written for those who had never seen an autopsy performed, who had no medical knowledge and very little intelligence. The book does contain many points of interest and of value to those interested in post-mortem examinations, but told with such unnecessary minuteness of detail as to detract from the general usefulness of the work. It is also over-illustrated, e. g.: After a careful description of the methods of opening the cadaver and removing the sternum, one scarcely needs thirteen photographs and three diagrams to make the matter plain and the book would have been as complete had the method of taking the rectal temperature of the guinea-pig been left to the ingenuity of the worker. But if one must have the illustrations, it would be more satisfactory to have them inserted opposite or at least near the text reference to them.

The very title of the book, "Post-mortem Pathology," and such chapter headings as "Micro-organismal diseases," and "Comparative post-mortems," lead one to expect the rather informal style and careless diction which he finds in the text. There are obscurities of meaning, and inaccuracies of statement which a careful writer would avoid.

Such are a few of the features which mar the book and which the second edition has not eradicated.

BOOKS RECEIVED.

Diseases of the Liver, Gall-Bladder and Bile-Ducts. By H. D. Rolleston, M. A., M. D. (Cantab.), F. R. C. P. Fully illustrated. 1905. 8vo. 794 pages. W. B. Saunders and Company, Philadelphia, New York, London.

Gall-Stones and Their Surgical Treatment. By B. G. A. Moynihan, M. S. (Lond.), F. R. C. S. Leeds. Fully illustrated. 1905. 8vo. 386 pages. W. B. Saunders and Company, Philadelphia, New York, London.

Diet in Health and Disease. By Julius Friedenwald, M. D., and Ruhräh, M. D. 1905. 8vo. 689 pages. W. B. Saunders and Company, Philadelphia, New York, London.

A Manual of Personal Hygiene. Proper Living upon a Physiological Basis. By American Authors. Edited by Walter L. Pyle, A. M., M. D. Second edition, revised and enlarged. 1904. 8vo. 441 pages. W. B. Saunders and Company, Philadelphia, New York, London.

Saint Thomas' Hospital Reports. New Series. Edited by Dr. H. P. Hawkins and Mr. W. H. Battle. Volume XXXII. 1903. 8vo. 463 + 136 pages. 1904. J. & A. Churchill, London.

Scientific Memoirs. By Officers of the Medical and Sanitary Departments of the Government of India. No. 12. *On the Morphology, Teratology, and Declinism of the Flowers of Cannabis.* By Major D. Prain, M. B., I. M. S. 1904. 4to. 32 pages. Office of the Superintendent of Government Printing, Calcutta, India.

Twenty-first Annual Report of the Bureau of American Ethnology to the Secretary of the Smithsonian Institution. 1899-1900. By J. W. Powell, Director. 1903. 4to. 360 pages. Government Printing Office, Washington.

Twenty-second Annual Report of the Bureau of American Ethnology to the Secretary of the Smithsonian Institution. 1900-1901. By J. W. Powell, Director. Part I. 1904. 4to. 320 pages. Government Printing Office, Washington.

A Treatise on Diseases of the Nervous System. By L. Harrison Mettler, A. M., M. D. Complete in one volume. Profusely illustrated. 1905. 4to. 989 pages. Cleveland Press, Chicago.

A Text-Book of Histology, Including Microscopic Technic. By A. A. Böhm, M. D. and M. von Davidoff, M. D. Edited, with extensive additions to both text and illustrations. By G. Carl Huber, M. D. Second edition, thoroughly revised and enlarged. With 377 illustrations. 1904. 8vo. 528 pages. W. B. Saunders and Company, Philadelphia, New York, London.

American Ophthalmological Society. Transactions of the fortieth annual meeting. Volume X, Part II. 1904. 8vo. Published by the Society, Hartford.

Medical Communications of the Massachusetts Medical Society. Volume XIX, No. III. 1904. 8vo. Boston.

The Practical Application of the Röntgen Rays in Therapeutics and Diagnosis. By William Allen Pusey, A. M., M. D. and Eugene Wilson Caldwell, B. S. Second edition, thoroughly revised and enlarged. 1904. 8vo. 690 pages. W. B. Saunders and Company, Philadelphia, New York, London.

Atlas and Epitome of Operative Ophthalmology. By Prof. Dr. O. Haab, of Zurich. Authorized translation from the German with editorial notes and additions. Edited by G. E. de Schweinitz, A. M., M. D. With 30 colored lithographic plates and 154 text-cuts. 1905. 12mo. 377 pages. W. B. Saunders and Company, Philadelphia, New York, London.

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CONTENTS.

PAGE

Vaginal Cysts. By Thomas S. Cullen, M. B., ... 207

The Etiology and Pathogenesis of Pernicious Anæmia. By C. H. Bunting, M. D., ... 222

Recurring Phlebitis of Obscure Origin. By John Bradford Briggs, M. D., ... 228

A Report of Some Observations on Heart Block in Mammals. By Joseph Erlanger, M. D. 234

The Force of Contraction of the Gall-Bladder and the Course of its Motor and Inhibitory Nerve Fibers. By J. A. Freese, . . . 235

PAGE

Proceedings of Societies:

The Johns Hopkins Hospital Medical Society, ... 237

Sarcomatous Myoma; Fibroma of Abdominal Wall; Primary Carcinoma of the Fallopian Tube; Accessory Omentum [Dr. Cullen];—The Electrical Theory of Matter [Dr. Jones];—Experiments on Amphibian Embryos [Dr. Lewis];—Comparative Surgery [Dr. Cushing].

Notes on New Books, ... 239

VAGINAL CYSTS.

By Thomas S. Cullen, M. B.

Associate Professor of Gynæcology in the Johns Hopkins University; Associate in Gynæcology, Johns Hopkins Hospital.

Vaginal cysts have long been recognized and accorded a very thorough consideration. Among the more important contributions on this subject are the articles of Breisky, v. Winckel, Freund, Veit, Stokes, Gebhard, and Bandler. In Vol. VII of the Johns Hopkins Hospital Reports Ernest Stokes gave a careful résumé of the literature and reported eleven cases. Since that time many new specimens have been received so that the total number examined at the hospital including those reported by my colleague Stokes amounted to fifty-three on January 1, 1904. In order to facilitate a satisfactory consideration of the subject it may be well to speak briefly of (1) the gross and histological anatomy of the normal vagina; (2) the embryonic structures that may persist in the vagina; (3) changes in the vagina incident to vaginitis; (4) changes due to injuries resulting from childbirth; (5) alterations in the vagina caused by perineal operations; (6) the relation of the urethra to the vagina.

(1) The Normal Vagina.

The lining of the cavity is composed of several layers of squamous epithelium of which the more superficial near the outlet tend to become horny. The deepest layer which rests on the underlying stroma consists of cells, cuboidal or low cylindrical in type. The stroma is made up of fibrous tissue poor in cell elements, but as a rule with a well-developed blood supply. Small tufts of the stroma project up into the epithelium producing the so-called papillæ. The vaginal mucosa resembles very closely the normal skin. The pigment in the deep layers is, however, usually wanting.

Vaginal Glands.—The existence of vaginal glands has been much questioned, but v. Preuschen in 1877 after a careful examination of thirty-six bodies found definite vaginal glands in four. The necks of these glands are lined by squamous epithelium, while the deeper portions, which spread out into definite bays, are lined by cylindrical epithelium on which cilia may be detected. Opening into the dilated glands are little crypts. Similar glands had previously been noticed in 1870 by Hennig. In Path. No. 955, where we were dealing with a small cyst 6 mm. in diameter and lined by one layer of cuboidal epithelium, I found a small oval gland-space lined with one layer of high cylindrical epithelium (Fig. 1). It closely resembled a cervical gland and was surrounded by a definite inflammatory zone.



FIG. 1.—A VAGINAL GLAND (10 DIAMETERS).

Gyn.-Path. No. 955. Lying beneath the slightly atrophic mucosa, is a vaginal cyst, 6 mm. in diameter. Immediately beneath the vaginal epithelium is a small gland. This was lined with high cylindrical epithelium resembling that of a cervical gland. The dark areas (*a*) represent small masses of normal vaginal epithelium.

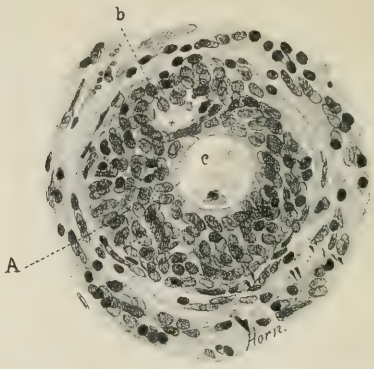


FIG. 2.—UNUSUAL EPITHELIAL ELEMENTS IN THE POSTERIOR VAGINAL WALL (480 DIAMETERS).

In this case there was a complete perineal tear with two minute vaginal cysts lined with squamous epithelium. In the immediate vicinity was the nest of cells which are seen at *A*. These cells have oval nuclei and show a distinct glandular arrangement (*b* and *c*). Surrounding this group of cells is the ordinary connective tissue of the vagina.

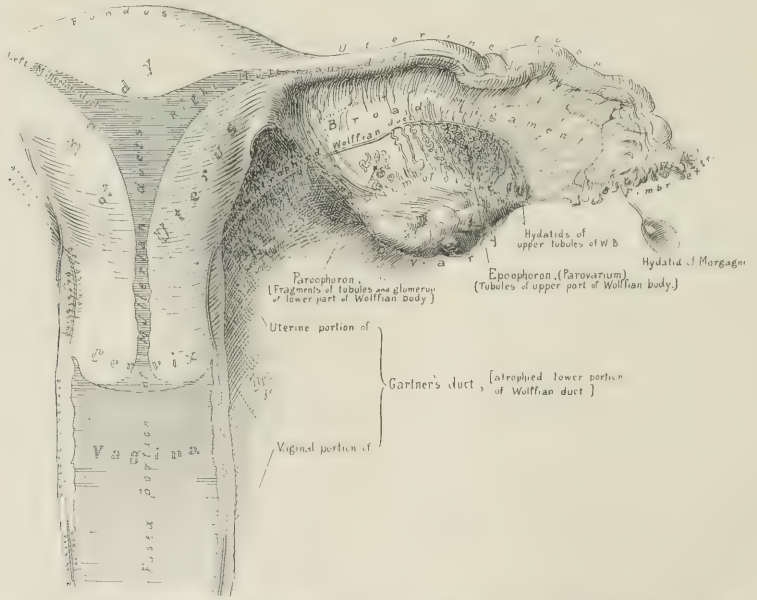


FIG. 3.—A SCHEMATIC ILLUSTRATION OF THE FORMATION OF THE UTERUS, THE TUBES, AND THE VAGINA, AND OF THE RELATION OF THE WOLFFIAN AND GARTNER'S DUCTS TO THE BROAD LIGAMENT, UTERUS AND VAGINA.

The outer portions of Müller's ducts form the Fallopian tubes. The middle portions unite to form the uterus and the distal portions form the vagina. In the broad ligament between the tube and ovary we see the epoophoron or parovarium composed of many cork-screw-shaped tubules and communicating along the upper extremities with the collecting duct. They represent the tubules of the upper part of the Wolffian body. Lying embedded at the inner side of the hilum of the ovary are fragments of tubules and glomeruli of the lower part of the Wolffian body. In the drawing Gartner's duct can be traced obliquely down through the broad ligament into the uterus near the internal os. It can be followed through the outer portion of the cervix to the vagina. As a rule, the vaginal, uterine, and inner broad ligament portions disappear.

We were unable to tell whether the cyst was situated in the anterior or posterior vaginal wall.

In Path. No. 5593 there was a complete tear of the perineum and situated in scar tissue were two minute vaginal cysts lined with squamous epithelium. In the vicinity can be seen an almost circular nest of cells with oval vesicular nuclei (Fig. 2). In this mass of cells are two definite gland-spaces around which the cells appear to be cuboidal or low cylindrical in type. We are at a loss to explain the presence of this group of cells, particularly as they were situated in the posterior vaginal wall where a complete tear existed. They were too far away from the rectum and surrounded by too broad a zone of fibrous tissue to have originated in any way from the bowel. Furthermore their appearance did not suggest any relationship to rectal epithelium.

From the foregoing there seems to be no doubt that vaginal glands exist in a moderate percentage of women.

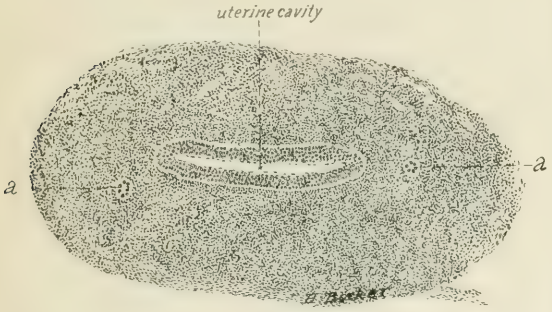


Fig. 4.—A Cross Section of the Uterus near the Cervix Showing Gartner's Duct on each Side of the Uterine Cavity (Fetus at the end of 3d month).

The uterine cavity is represented by a long slit lined by several layers of epithelium. Gartner's ducts are situated well toward the outer side of the uterus, are circular and lined with one layer of cuboidal epithelium. The uterine muscle is not as yet well differentiated.

(2) Embryonic Structures that may persist in the Vagina.

(*a*) Gartner's duct.

(*b*) Remains of Müller's duct.

(*c*) Misplaced ureter.

(*a*) *Persistence of Gartner's Duct.*—In the embryo remains of the Wolffian body are recognized as the parovarial tubules situated between the tube and ovary. The duct is continued downward through the broad ligament along the side of or in the substance of the uterus as Gartner's duct. It lies in the substance of the cervix near its outer side and then extends down the anterior or lateral wall of the vagina nearly to the outlet (Fig. 3).

In Fig. 4 we have a cross-section of the uterus in a human embryo at the end of the third month. On either side of the uterine cavity a cross-section of Gartner's duct is clearly shown.

Although it is sometimes possible to trace the duct nearly its entire length in the human being, as a rule, only the upper portion is visible, and this in time usually disappears. The structure is best studied in the cow, as in this animal the duct is easily traced. Bland-Sutton gives us a very good illustration (Fig. 5) of Gartner's duct extending down the side of the cervix and in the lateral wall of the vagina forming two distinct cystic dilatations.

Remnants of Gartner's duct are sometimes recognized as one or more disconnected segments following the usual course of the duct along the lateral wall or roof of the vagina to

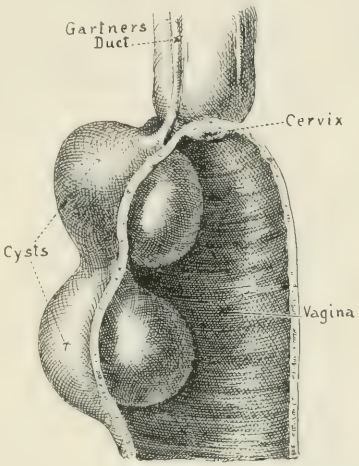


Fig. 5.—Vaginal Cysts in a Cow; due to Dilatations of Gartner's Duct.

Passing down the outer side of the cervix are Gartner's ducts. The duct on the left shows two distinct dilatations in the vagina producing typical vaginal cysts (Re-drawn after Bland-Sutton. Published by Keener & Co., Chicago, 1903).

the cervix. In some instances it has been possible to trace the duct from the vagina up to the parovarium. In other words, it was patent for its entire length.

A cross-section of the duct will show an outer covering of fibrous tissue, a middle zone of non-striped muscle arranged longitudinally, transversely or running in both directions, and an inner lining of one layer of cuboidal or cylindrical epithelium.

(*b*) *Remains of Müller's Ducts in the Vagina.*—In some instances Müller's ducts fail to meet. We then may have two uteri and two vaginæ. In other cases the ducts are separate in their upper portions and partially unite at the cervix.

Thus we may have a bicornate uterus with two cervices and two vaginæ or a bicornate uterus with one cervix and one vagina. Other minor variations resulting from failure of Müller's ducts to unite occur, but we are here chiefly interested in the variety where one uterus is fairly well developed, while a second is represented by a rudimentary cord or a

very imperfectly formed organ. The corresponding vagina becomes fused with the lateral wall of the well-developed one. Secretions accumulate in this rudimentary vagina, until it resembles a cystic tumor springing from the lateral wall of the vagina (Fig. 6).

Sometimes its accompanying uterus has been fairly well developed and may communicate with it. In these cases the retained menstrual flow distends the blind vaginal pouch and when the sac is opened, it is found filled with chocolate-colored fluid (Fig. 7). Sometimes the tension becomes so great that eventually a small opening forms and the fluid escapes through the vagina. Such sacs may also become infected before they open. Attention to these rudimentary vaginæ situated in the wall of a well-developed vagina was directed by W. A. Freund in 1877. In his paper he reported several such cases. Kleinwächter shortly after Freund's article reported similar instances.

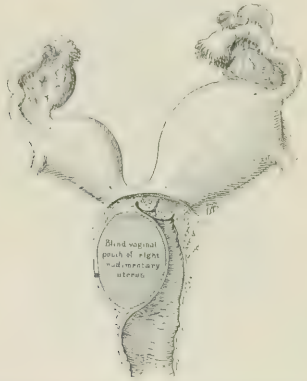


Fig. 6.—Rudimentary Vagina in the Wall of a Well Formed Vagina.

A schematic illustration of a blind vaginal pouch due to imperfect union of Müller's ducts. The left uterus is well developed and its corresponding vagina perfectly formed. The right uterus is rudimentary and in its cervical portion is represented by a solid cord. The vagina is seen as a blind cystic pouch. Such cavities may collapse, but if distended contain quantities of exfoliated squamous epithelium.

(*c*) *Abnormal Relation of the Ureter to the Vagina.*—When the ureter is in its normal situation its relation to the vagina is not an intimate one, but occasionally a case is met with in which in one lateral wall a small cystic prominence is detected, from which when opened an escape of urine takes place. In other rare instances a fistulous opening into the lateral vaginal wall has been found through which there was a constant discharge of urine. Where any history of injury to the vagina is excluded, which could possibly have caused a fistulous opening between the normal ureter and the vagina, we are probably dealing with an embryonic abnormality. The latter alternative is more probable where there is a double ureter on the one side. Broedel and others have pointed out that where two ureters and two kidneys exist on one side the ureter from the lower kidney is usually inserted at the normal site, while the one connected with the upper kidney is carried down further with the Wolffian duct and is inserted more medialward and nearer the inner urethral orifice. It only would be necessary for this second ureter to be carried down a little further to have it open into or form a blind pouch in the vagina.

(3) Changes in the Vagina incident to Vaginitis.

Adhesive vaginitis occasionally occurs, especially in young individuals. Here, as a result of an ulcerative process or a very severe grade of inflammation associated with loss of the vaginal epithelium, the vaginal folds become adherent to one another, producing blind pockets. Such a vaginitis may be due to a general systemic infection, to gangrene following the presence of a foreign body in the vagina or to the highly irri-

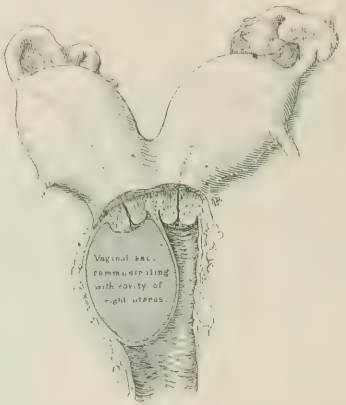


Fig. 7.—A Vaginal Pouch Communicating with its Uterus but not with the Well Formed Vagina.

A schematic representation of a condition that sometimes occurs where the vaginal portion of Müller's ducts have failed to fuse. The uteri have developed separately. The vagina proper has been formed from the lower portion of the left Müller's duct. The right vagina, although communicating with its corresponding uterus, has no outlet. The sac is invariably filled with chocolate-colored contents, the remains of menstrual blood.

tative urine where inflammation of the bladder exists. These vaginal occlusions may have a definite bearing on the future development of vaginal cysts.

(4) Changes in the Vagina due to Injuries at Childbirth.

The different degrees of laceration of the perineum during labor are well known. Sometimes without any external laceration there may be one or more tears in the mucosa within the outlet. Again there may be a minor or a very extensive laceration of the entire perineum. In many cases, not only are the tears deep but the injury has occurred in such a manner that little tags of mucosa lie partially detached, and during the subsequent healing of the perineum these may

be turned in and included between the edges of the wound. Under these circumstances we have squamous epithelium buried in the perineum; that is, lying in the tissue from 1 to 5 mm. beneath the surface. A similar fate of the small tags of mucosa may also follow even when the perineum is immediately repaired.

(5) Alterations in the Continuity of the Vaginal Mucosa caused by Perineal Operations.

Where it is deemed advisable to repair the outlet some time after labor, after having mapped out a line of denudation it is necessary to remove a large area of vaginal mucosa. But if this is cut away piecemeal instead of in long strips or where the field of operation is not kept perfectly clear, small fragments of the mucosa may be left behind (Fig. 8).

When the edges of the wound are approximated these islands of mucosa lie more or less deeply embedded in the underlying stroma and entirely cut off from the parent mucosa.

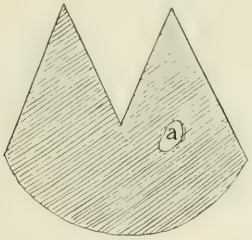


Fig. 8.—A Fragment of Vaginal Mucosa that may give rise to an Inclusion Cyst.

The sketch gives the usual outlines of denudation in a perineal operation. At *a*, a small island of mucosa has been overlooked. When the parts are brought together this will lie deeply embedded and could readily be the starting point of a vaginal cyst.

(6) The Relation of the Urethra to the Vagina.

It is very important to have a clear understanding of the relation of the vagina to the urethra, as over a considerable distance they are intimately associated. Furthermore, as will be seen later, certain cyst-like dilatations arising from the floor of the urethra should not be confused with vaginal cysts although at first sight they may bear a striking similarity. Disse in v. Bardeleben's Anatomy has given us a very clear description of the urethra which I will quote: "The posterior wall of the urethra is firmly attached to the anterior vaginal wall throughout its entire length. Both canals run parallel to each other. The epithelium of the urethra is about .1 mm. thick. The superficial layers of cells are all composed of squamous epithelium. The cells of the deeper layers are more club-shaped. The mucosa is longitudinally folded and as a result club-shaped and tubular depressions are produced. Some of these are simple lacunæ, others are glandular in nature and secrete a colloid material which may in time form concretions. The lacunæ are found in the entire length of the urethra. The smaller ones are broad-based and open by a narrow channel into the urethra. The larger ones are tubular, push into the propria, often branch and tend to run parallel with the surface. These are the glands that sometimes produce the hardened secretion. They are termed Littré's glands." On either side of the urethra are Skene's ducts, which must also be remembered in a consideration of vaginal cysts.

Vaginal Cysts.

It is rather difficult to classify all vaginal cysts according to their origin and the accompanying figures should be accepted only as representing an approximate ratio of the different varieties to each other. I have examined in all fifty-three cases and in a few of these two cysts were present in the same individual.



Fig. 9.—A Small Inclusion Cyst (natural size).

Gyn.-Path. No. 5509. A small piece of tissue from the floor of the vagina. It is traversed by several scars as is well seen at *a*. At *b* a small vaginal cyst projects slightly from the surface. In the deep tissue it spreads out. The cyst was lined with several layers of squamous epithelium.

Variety of Cysts.—In twenty-six the origin was clearly the result of a perineal tear or of a perineal operation.

Four seemed to originate from vaginal glands.

Eleven were apparently derivatives of Gartner's duct.

Three were situated near the external orifice of the urethra.

In eight it was impossible to determine the mode of origin.

Inclusion Cysts.—(Those due to small portions of the vaginal mucosa being included in the stroma.) Such cysts are relatively small and are naturally found in the posterior or in the lower lateral wall of the vagina. They are often situated in the scar tissue of an old tear (Fig. 9) or may form a globular mass projecting from the posterior vaginal wall and covered by normal vaginal mucosa (Fig. 10).

In our cases the cysts varied from 3 mm. to 2.5 cm. in diameter. The smaller ones were yellowish in color, the larger more whitish in appearance.

The cyst walls vary from 2 to 4 mm. in thickness; the inner surface is smooth. The cyst contents vary slightly. The smaller ones are often completely filled with a friable material which gives a yellowish tinge to the cyst. This at first sight

slightly resembles pus, but in reality represents masses of exfoliated squamous epithelium.

On histological examination the vaginal mucosa over the surface of the cyst is usually normal, but as might be surmised over the most prominent part it is often slightly atrophic. The cyst walls are composed of fibrous tissue; the inner surface is lined with a varying number of layers of squamous epithelium. Sometimes there is a uniform covering of from 2 to 30 layers of cells, but as a rule the epithelial lining is very thick at one part of the cyst and thin at a distant point. The superficial epithelial cells are often devoid of nuclei and are filled with vacuoles. The deepest layer is usually cuboidal.

The cysts contain desquamated squamous epithelium, detritus, and at times fat droplets and cholesterin crystals. Where the cysts are relatively large the cavity is often partially filled with clear fluid. These cysts are usually single, but they may be multiple, as in Path. No. 3321 (Fig. 11). Here we have three small irregular cysts separated by very slender partitions. They were lined with from 2 to 8 layers of squamous epithelium.



Fig. 10.—A Vaginal Cyst Occurring three Years after Repair of a Perineal Tear.

Gyn.-Path. No. 1504. This cyst contained clear fluid and was lined with several layers of squamous epithelium. It was probably an inclusion cyst.

As has been so clearly pointed out by Stokes and others, little doubt remains that these cysts originate from inclusions of the vaginal epithelium. Our own observations fully substantiate this view. In twenty-four out of the twenty-six of these cases we were able to get a satisfactory history and in every instance the patient had a lacerated perineum and in five out of the twenty-four the perineal tear extended into the rectum. In every case where the site of the cyst was noted it was found either in the posterior or lateral wall, usually in the floor of the perineum.

In Path. No. 298 I noticed a most unusual picture in the cyst wall just beneath the lining epithelium. Here the fibrous tissue was very dense and contained numerous giant cells, some with nuclei in the center of the cell, others with the nuclei arranged peripherally, while the centers of a few contained large, faintly granular masses. The picture in no way suggested tuberculosis.

Cysts probably originating from Vaginal Glands.—Cysts of this origin are apparently less common. Three of our cases seem to fall under this category and possibly a fourth. In Path. No. 2131 A there was a cyst, 6 mm. in diameter, situated in the scar tissue of an old perineal tear. It was lined with cuboidal or almost flat epithelium. Associated with it was a small cyst of exactly the same size and lined with several layers of squamous epithelium. The first cyst, from its situation and epithelial lining, was in all probability a cystic vaginal gland. In Path. No. 2133 B there was also a small cyst in the posterior vaginal sulcus lying near the scar in an old perineal tear and lined with cuboidal cells. The cyst cavity was partly filled with mucus. In this case also there was a small accompanying inclusion cyst. Path. No. 2890 affords another example of a cystic vaginal gland. Here in the scar tissue of the vagina was a cyst 1.5 cm. in diameter lined with very low cuboidal epithelium which secreted mucus.



Fig. 11.—Multiple Vaginal Cyst (6 diameters).

Gyn.-Path. No. 3321. These cysts were associated with a perineal tear, were situated in the left vaginal wall and were lined with from two to eight layers of squamous epithelium. The lower two are irregular in outline and have little tufts of stroma projecting into them.

In Path. No. 2930 there had been a complete tear of the perineum. There were two very small vaginal cysts lying side by side and lined with cuboidal epithelium (Fig. 13). These were probably cystic vaginal glands, but this is only surmise as the exact position of the cyst was not given. In Path. Nos. 2131 A and 2133 B and 2890 I think we have a right to assume that the cysts were derived from the vaginal glands, since with the exception of the latter no other cylindri-

cal or cuboidal epithelial structures are found in this region. Of course it might be said that the cyst was primarily lined with squamous epithelium and that this had exfoliated, leaving only the deepest layer of cuboidal cells; but had this been the case, we would still find evidence of exfoliated squamous epithelium in the cyst cavity. The most convincing evidence, however, is furnished by the fact that we have clear-cut types of two varieties of cysts, the inclusion cyst and that derived from vaginal glands lying side by side without any evidences of degenerative changes in either of them.

Cysts of Gartner's Duct.—As has already been pointed out, in the fœtus Gartner's duct may in some instances pass from the parovarium down the side of or in the substance of the



Fig. 12.—A Small Vaginal Cyst Embedded in Scar Tissue (40 diameters).

Gyn.-Path. No. 3690. The cyst was 1.5 cm. in diameter, associated with a perineal tear and embedded in scar tissue. It is lined with from 1 to 7 layers of fairly well defined squamous epithelium. It is situated at the bottom of the vaginal cleft (*a*) and probably at one time communicated with it.

uterus to the cervix and thence obliquely downward and inward to the hymen (Fig. 3). In the vagina its course may run just to the side of the urethra or in the lateral wall of the vagina. We also know that, while in the majority of cases this duct disappears, in a few instances isolated portions persist in adult life. Such isolated links of the persisting duct may as a result of accumulated secretions become cystic. Numerous such examples are on record. If only one segment of the duct persist, a single cyst develops, but should five or six be present, we may have a corresponding number of cysts which, as we should naturally suppose, occur in a single row. The cysts may be exceedingly small, but as a rule reach several centimeters in diameter. In rare instances they almost completely block the vagina. They naturally

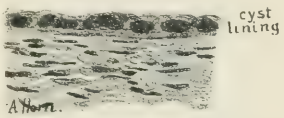


Fig. 13.—Epithelial Lining of a Small Cyst in the Posterior Vaginal Wall (480 diameters).

Gyn.-Path. No. 2930. The cyst lining consists of one layer of cuboidal cells with oval nuclei. These rest on the connective tissue stroma forming the cyst wall.

have an outer covering of vaginal mucosa which over the most prominent part may be atrophic. The cyst walls are usually not more than 1 or 2 mm. in thickness. The inner surface

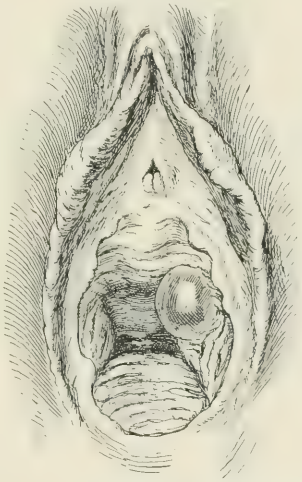


Fig. 14.—Vaginal Cysts, Probably Originating from Gartner's Duct (natural size).

Gyn.-Path. No. 3107. The cyst is situated in the left side of the vaginal vault just within the vaginal orifice. It has a smooth surface, its inner surface was lined with one layer of cuboidal cells. Its situation strongly suggests an origin from Gartner's duct.

of the cyst may be perfectly circular, but is frequently oblong and now and then a cyst is met with in which there is a small stem, as it were, leading off from the main cyst (Fig. 16). Such a finding would demonstrate fairly conclusively that a portion of the duct has not yielded so readily to the process of dilatation.

The inner surface of the cyst may be perfectly smooth along its convex vaginal surface, and yet present a definite undulating surface on the opposite or fixed side, showing clearly an unequal dilatation and differing thus from an ordinary cyst. Fig. 17 demonstrates this clearly.

Occasionally we meet with an oblong cyst, as in Path. No. 1775, where the tumor measured 8 x 5 cm. The inner surface presented a definite wavy appearance, being gathered up



Fig. 15.—Cyst in the Anterior Vaginal Wall.

Gyn.-Path. No. 640. Situated beneath the urethra is a translucent cyst. On being dissected out this was found to measure 4.5 × 3.5 cm. Its inner surface was smooth and glistening and it was lined with one layer of flat cells. This cyst was in all probability a dilated portion of a Gartner's duct.

into large and small folds. The cysts are invariably translucent and contain a clear straw-colored or pale fluid.



Fig. 16.—Small Cyst Showing Irregular Dilatation.

Gyn.-Path. No. 2878. Covering the surface is vaginal mucosa. The cyst has a smooth inner surface but has distended unevenly. For example, at *a* there is a little pocket that projects downward from the main cyst. Such pictures are relatively common in cysts of Gartner's duct, as one portion of the duct may dilate more than a neighboring segment. The cyst was lined with one layer of cylindrical epithelium. For a low power picture see Fig. 17.

In eleven of our cases a dilatation of a portion of Gartner's duct appears to have been responsible for the cyst. In ten of these the position of the cyst was ascertained. In the remaining one the anatomical peculiarities afforded a sufficient clue for the diagnosis. The most common situation was in the anterior vaginal wall just behind the urethral orifice.

As regards ten of our cases the distribution was as follows:

In the anterior vaginal wall near the urethra, six cases.

In the right lateral vaginal wall, one case.

In the left vaginal wall, one case.

In the right vaginal fornix, one case.

In the left vaginal fornix, one case.

Fig. 15 is a characteristic example of a cyst situated just beneath the urethra. Only rarely do the cysts become pedunculated. Where the cyst is situated in the vaginal fornix

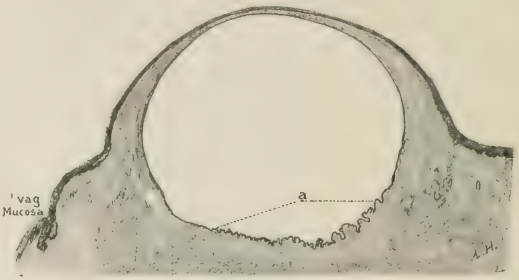


Fig. 17.—Vaginal Cyst, Probably Originating from Gartner's Duct (6 diameters).

Gyn.-Path. No. 2878. For the natural size see Fig. 16. Covering the surface of the cyst is the vaginal mucosa. This at the sides is normal, over the most prominent part atrophic. The free side of the cyst is smooth, that on the fixed side is gathered up into the folds as shown at *a*. Where inclusion cysts or cysts originating from vaginal glands exist there is equal distension.

the walls are liable to be considerably thicker as the duct lies more deeply embedded in the tissue.



Fig. 18.—A Cyst of the Anterior Vaginal Wall.

Gyn.-Path. No. 4644. *A* is a 15 diameter enlargement of the wall. The outer vaginal covering (*a*) is normal. The walls (*b*) are composed of fibrous tissue and the inner surface (*c*) has a delicate lining. *B* is a 408 diameter picture of a portion of *A* and at *d* one sees the inner cyst lining composed of a single layer of cuboidal epithelium.

The cyst walls proper are composed of fibrous tissue; sometimes intermingled with these are bundles of non-striped muscle fiber. These were demonstrated in two of our cases. Where the cyst is small it is often possible to make them out, but in those of large size the muscle is so spread out that sections from various portions of the wall often fail to reveal it although at other points it may be present. The inner surface of the cyst is lined with one layer of cylindrical, cuboidal, or almost flat epithelium.

In the majority of our cases the epithelial lining consisted of cuboidal cells, in three cases of cylindrical and in one of flat cells.

A Very Unusual Cyst occurring high up in the Vaginal Fornix.—Path. No. 1850 must, I think, be included under those probably arising from Gartner's duct on account of its location—the right vaginal fornix. It, however, presents a most unusual histological picture.

The cyst was 1 cm. in diameter with walls 5 mm. thick. Projecting from its inner surface were dome-shaped elevations fully 2 mm. in length (Fig. 19).

The vaginal mucosa over the cyst is atrophic but normal. The walls are composed of fibrous tissue. The dome-like elevations are newly formed, consisting of small, round cells and many young capillaries. This tissue is permeated by polymorphonuclear leucocytes. Just beneath the inner surface is a well-defined gland-like space lined with cylindrical epithelium.

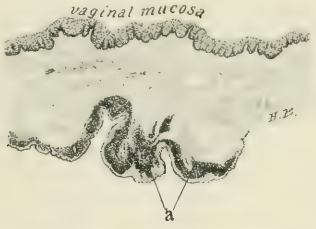


Fig. 19.—Dome-like Elevations Projecting into a Vaginal Cyst (4 diameters).

Gyn.-Path. No. 1850. The cyst was situated in the right vaginal fornix. The vaginal mucosa over the cyst is normal. The walls are composed of ordinary connective tissue. Projecting into the cavity are the dome-shaped elevations *a*. These are composed of small round cells and young capillaries. For the character of the cyst lining see Fig. 20. Over these dome-like elevations are from 20 to 30 layers of squamous epithelium.

The lining of the cyst varies much in different places. Over the dome-shaped elevations are from two to twenty layers of squamous epithelium. At other points are definite finger-like folds with gland-like depressions between them (Fig. 20). The folds and the clefts between them are lined with one layer of cylindrical or cuboidal epithelium and have oval nuclei situated near the base of the cell. A slight inflammatory change is evident, as polymorphonuclear leucocytes and small round cells are seen between the epithelial cells

While this case is in all probability rightly classed with those having their origin from Gartner's duct, the histological picture is certainly difficult of explanation. This cyst gives no evidence whatever of malignancy. Such gland-like spaces may, however, account for the occasional primary adeno-carcinomata that develop in the vagina. In rare instances, as pointed out by Veit and mentioned elsewhere, Gartner's duct is patent all the way from the parovarium to the vagina. Cystic dilatation of the entire duct occasionally occurs, and as a result we have a vaginal cyst filled with clear fluid and extending up along the side of the uterus to the parovarium. This might well be termed a vagino-parovarial cyst. When of moderate size it will occupy one side of the vagina, but when very large, it will occupy not only the lateral wall but also encroach on the anterior and posterior surfaces of the vagina. The cyst contents are usually clear and watery, but if there has been hæmorrhage into the cavity, they are chocolate-colored. At times these cysts are only partially filled with fluid. Accordingly if pressure be exerted on the vaginal portion it collapses, the parovarial segment meantime becoming tense. On the other hand, if pressure be made over the parovarium, the tumor mass in this situation disappears and the vaginal portion becomes distended. In none of our cases did we find evidence of a patent Gartner's duct.

Vaginal Cysts arising from Urethral Glands. If vaginal



Fig. 20.—Epithelial Lining of a very Unusual Vaginal Cyst (50 diameters).

Gyn.-Path. No. 1850. This cyst was 1 cm. in diameter and situated in the right vaginal fornix; at *a* we have a lining of one layer of high cylindrical epithelium which at *b* seems to have proliferated resembling squamous epithelium. In the vicinity of *c* there are distant finger-like ingrowths lined with one layer of low cylindrical epithelium and at *d* there is a definite gland-like space. At *e* the cyst is lined with many layers of cells resembling squamous epithelium. A typical transition epithelial lining is seen at *f*,—a superficial layer of low cylindrical cells resting on several layers resembling squamous epithelium. The cyst walls show considerable inflammatory reaction, particularly noticeable at *g*.

cysts ever owe their origin to urethral glands, such a condition is of very rare occurrence. The possibility, however, cannot be excluded; in fact in two of our cases various histological appearances would justify the supposition that the tissue is very similar to, if not identical with, that of the urethra. In Path. No. 2870 we have a cyst, 1 x .5 cm., oval in form. The overlying vaginal mucosa is normal. The cyst walls are composed of fibrous tissue. The epithelial lin-

ing of the cyst presents a most unusual picture. It consists of from three to eight layers. The superficial layer is cylindrical and rests on the underlying layers of flattened and deeply staining cells. The general arrangement of the epithelium simulates that found in the urethra.

In Path. No. 1502 we have a cyst, 1 x 1.5 cm., in the anterior vaginal wall just within the hymen and to the right of the urethra. It is filled with clear fluid and has a delicate finger-like ingrowth. The cyst lining is composed of one layer of cylindrical ciliated epithelium (Fig. 21).

In the cyst wall is a definite gland-space lined with high cylindrical ciliated epithelium. It is just possible that in this case the cyst owes its origin to urethral elements. An origin from Gartner's duct can, however, equally well be claimed.

Although in both of these cases the features in the main would suggest their origin from urethral structures, the connecting link, namely the direct continuity with the urethra, is wanting.

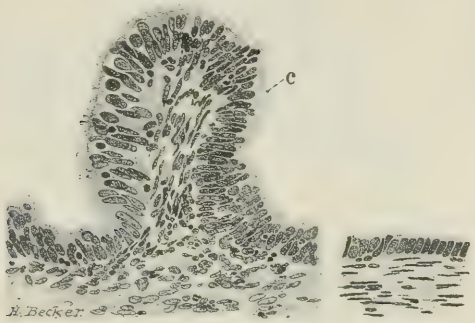


Fig. 21.—The Lining of a Cyst Situated in the Anterior Vaginal Wall (400 diameters).

Gyn.-Path. No. 1502. *A* is the small projection, covered by cylindrical ciliated epithelium. The stem of the projection is formed by young connective tissue cells. *B* represents a small portion of the cyst wall. The cyst has been cut at right angles and we see that it is lined with a single layer of cylindrical cells.

Unclassified Vaginal Cysts.—In nine of our cases owing to lack of clinical details it was impossible to venture a classification with any degree of certainty. In Path. Nos. 1470, 4060, 5792, 6274, and 2442 little is known of the clinical history. Path. No. 955 looks very much like a cystic dilatation of Gartner's duct. The cavity was lined with one layer of cuboidal epithelium.

In Path. No. 2010 the small cyst had a finger-like ingrowth and was lined with one layer of cylindrical epithelium. It probably also represented a dilated segment of the duct. Path. No. 5037 appeared to have a similar origin.

In Path. No. 4079 B the small cyst was lined with one layer of cuboidal epithelium and lay in close contact with an inclusion cyst. In all probability it was a dilated vaginal gland.

Gas Cysts in the Vagina.—Various names, such as colpohyperplasia cystica and colpitis emphysematosa, have been applied to this affection, which has been accurately described by v. Winkel. This condition is usually associated with pregnancy and consists of small cystic dilatations occurring usually in the submucosa, but occasionally in the epithelium itself. On puncturing the cyst there is a report with the escape of gas and the cyst collapses. Such cysts only last for a short time and then disappear.

v. Winkel in 1886 reported three observations in pregnant women. In a space that could be covered by a dollar he found fifteen to twenty cysts. All were superficial and transparent. The mucosa in which these were embedded was hyperæmic and succulent and the cysts were filled with gas. On puncture there was a loud noise with an escape of gas. C. Braun in 1861 recorded similar instances. According to Eisenlohr the cause of this disease must be a gas-producing micro-organism which stretches the lymph vessels and forces the lymph and organisms into the surrounding tissue. According to Strauss, as quoted by Veit, the cysts were usually surrounded by connective tissue, rarely by epithelium. Their occurrence seems to be analogous to that of gas cysts in the liver and other organs, and we should not be surprised if in the near future Welch's *B. ærogenes capsulatus* should be proved to be the causative factor. No treatment is necessary, as the cysts are of short duration.

Echinococcus Cysts.—In countries in which the echinococcus is prevalent, cysts may develop in the tissue between the rectum and vagina. They may project into the vagina and resemble vaginal cysts. If a doubt as to their nature exists a careful microscopical examination of the cyst contents or of its wall will render the diagnosis clear.

Clinical History of Vaginal Cysts.—All of the cysts in our cases were relatively small, and naturally gave rise to no symptoms whatever. In fact they were detected during examinations for some other trouble, or, as in case of inclusion cysts, during operations for perineal tears. Undoubtedly many of the smaller cysts are overlooked as in the ordinary routine laboratory examinations we have found some of which no account had appeared in the clinical record. Cysts 6 to 8 cm. in diameter partially block up the vagina and may interfere with coitus. If situated in the posterior wall they may roll the pelvic floor out in such a manner that at first sight prolapsus of the vagina may be diagnosed.

Cysts of the posterior wall have, in a few instances, formed effectual barriers to delivery. In Peter's case, for example, the cyst contained about one pound of clear fluid, and had to be evacuated with the trocar before labor could proceed normally.

In the case of a vagino-parovarial cyst which is not full mere pressure is sufficient to remove the obstruction, the fluid passing up to the parovarium and the vaginal portion collapsing into a flaccid pouch.

Vaginal cysts in the posterior wall may have to be differentiated from an abscess in the recto-vaginal septum. The cysts are not tender. Abscesses are painful, of rapid develop-

ment, and are accompanied by fever. In the lateral wall a vaginal cyst may be mistaken for a blind vagina. The thick walls of the occluded and imperfectly developed vagina and the fact that the uterus is imperfectly developed will usually suffice to render the diagnosis clear.

A suburethral abscess may bear a striking resemblance to a vaginal cyst. In this case, however, pressure on the abscess will be followed by an escape of pus from the urethra and by collapse of the sac.

Treatment.—The smaller cysts are excised and the resultant cavity sutured. Where it is somewhat large and removal is difficult, half or three-quarters of the cyst, according to circumstances, may be cut off, and the edge of the vagina united with that of the cyst on all sides. The remaining portion of the cyst thus becomes a part of the vagina and gradually unfolds until it is scarcely recognized. Where the cyst is of the vagino-parovarial type drainage or a combined abdominal and vaginal removal is necessary. It is, however, seldom wise to resort to an abdominal operation, unless there are pressure symptoms or the cyst is very annoying. A small dilated blind ureter must always be borne in mind when removal of cysts in the lateral or anterior wall is contemplated.

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ANALYSIS OF VAGINAL CYSTS OBSERVED AT THE JOHNS HOPKINS HOSPITAL DURING THE PERIOD 1893 TO JANUARY 1, 1904.

[If the reader wishes further particulars about the drawings in the text they will in most instances be found in this tabulated list of the cases. For example, Fig. 1 is from Gyn. Path. No. 955; on referring to this table Gyn. Path. No. 955 is readily found in the first column; the chief clinical features of the case together with the gross and histologic appearances of the cyst are also given.]

Gyn. Path. No.	Clinical No.	Age.	White or Black.	Para.	Perineal tear.	Previous perineal operation.	No. of cysts.	Site of cysts.	Size.	Shape.	Thickness of cyst wall.	Cyst contents.	Inner surface of cyst.	Condition of overlying vaginal mucosa.	Composition of cyst wall.	Epithelial lining of cyst	Cyst contents (microscopic).	Remarks.
509	3170	30	White.	2	Complete.		..		1.5 cm.	Irregular, globular.		Creamy yellow.		Slight thickening with faint downgrowths.	Connective tissue.	Squamous epithelium, 5 to 30 layers.		Negative on slide and culture.
640	3398	29	Black.	..	..		1	Just beneath urethra and 2.5 cm. with in vagina.	4.5x3.5 cm.		1-2 mm.	Transparent.	Smooth and glistening.	Atrophied.	Connective tissue; rich blood supply: small round-cell infiltration beneath surface.	One layer of flat epithelium.		
648	3402	36	White.	7	Yes.	0	1	Ant. vaginal wall.	1.5 cm.	Globular.	1.5 mm.	Transparent.	Smooth and glistening.	Normal.	Fibrous tissue and non-striped muscle fibers.	One layer of cylindric epithelium.		Stokes' drawing
955	236 San.	..	"	..	"	0	1		6 mm.	Globular.	0.5 mm.	Transparent.	Smooth	Normal, thickening at one point.	Fibrous tissue; contains gland resembling cervical gland in lining and secretion; is surrounded by inflammatory zone.	One layer of cuboid epithelium.		

ANALYSIS OF VAGINAL CYSTS OBSERVED AT THE JOHNS HOPKINS HOSPITAL DURING THE PERIOD 1893 TO JANUARY 1, 1904.—*Continued.*

Gyn. Path. No.	Clinical No.	Age.	White or Black.	Para.	Perineal tear.	Previous perineal operation.	No. of cysts.	Site of cysts.	Size.	Shape.	Thickness of cyst wall.	Cyst contents.	Inner surface of cyst.	Condition of overlying vaginal mucosa.	Composition of cyst wall.	Epithelial lining of cyst.	Cyst contents (microscopic).	Remarks.
1411	4834	36	"	6	"	Repaired in 1890.			2.5 cm.		2 mm.			Normal on sides, total absence over prominent part; no evidence of inflammation where epithelium is missing.	Fibrous tissue; considerable muscle; small round-cell infiltrat'n beneath cyst epithelium.	Several layers of squamous epithelium.	Swollen fatty epithelial cells, many polymorphonuclear leukocytes and small round cells.	Stokes' drawing.
1470																		
1502	4928	41	"	6	"		1		8 mm.									Details missing.
	4971	..	"	..	"		2	Just within right vaginal wall in sulcus.	1x1.5 cm. 0.5 cm.			Clear fluid.	Very small, finger like ingrowth.	No vaginal mucosa.	Fibrous tissue; small gland in wall, lined by one layer of cylindric epithelium.	One layer of columnar cells.	Some desquamated epithelial cells; some cells filled with yellow chromatin droplets.	Stokes' drawing.
1504	4973	..	"	6	"	Repaired 3 yrs. ago.	1	Posterior wall near outlet.	2.2 cm.			Transparent fluid.			Fibrous tissue; some small round cell infiltration of wall.	Squamous epithelium; in places 10 to 12 layers; where stroma is absent cells are swollen and filled with brown pigment.		
1518	4996	..	"	Yes.	Complete.		1	Posterior just to right of median line.	2x1.5 cm.	Globular.	1 to 3 mm.			Atrophy over prominent part, normal on sides.	Fibrous tissue.	Squamous epithelium, 1 to 7 layers; in places low cuboid.		
1562		..		..	..		..							Normal.	Fibrous tissue.	One layer cuboid cells.		
1775	Specimen.	.	White.	..	Yes.		1	Anterior vaginal wall.	8x5 cm.		3 mm.			Normal.	Fibrous tissue; convoluted cyst-wall lined by high cylindric epithelium; evidently due to downward projections of crypts.	One layer high cylindric; nucleus at base as in cells from cervix; in places cells cuboid; crypts present in walls.		Stokes' drawing.
1789	San.	..	.. .	.	..		1	Left vaginal wall.	1x2 cm.				Smooth and glistening.	Normal.	Fibrous tissue.	10 to 20 or more layers squamous epithelium.		
1850	5400	29	White.	0, married.	No.	No.	1	Right side high up.	1 cm.		5 mm.		Dome-shaped elevation 2x2 mm.	Thickened but normal.	Thickened just beneath mounds; great small round-cell and polymorphonuclear infiltration with new capillaries, gland-like space lined by cylindric epithelium just beneath inner surface.	Over mounds lining of from 2 to 20 or more layers squamous epithelium; in places definite finger-like folds with gland-like depressions, one covered by a layer of perfectly cylindric epithelium; nuclei oval and near base; between epithelial cells, mono- and polymorphonuclear leukocytes.	Some polymorphonuclear leukocytes.	
2010	Specimen.	..	...	..	..		1		5 mm.	...	1 mm.			Normal.		One layer cuboid or low cylindric epithelium; small finger-like ingrowths covered by cylindric epithelium.	Desquamated epithelium.	

ANALYSIS OF VAGINAL CYSTS OBSERVED AT THE JOHNS HOPKINS HOSPITAL DURING THE PERIOD 1893 TO JANUARY 1, 1904.—*Continued.*

Gyn. Path. No.	Clinical No.	Age.	White or Black.	Para.	Perineal tear.	Previous perineal operation.	No. of cysts.	Site of cysts.	Size.	Shape.	Thickness of cyst wall.	Cyst contents.	Inner surface of cyst.	Condition of overlying vaginal mucosa.	Composition of cyst wall.	Epithelial lining of cyst.	Cyst contents (microscopic).	Remarks.
2131	5835	28	White.	1	Yes.	0	2	A, posterior r. side 2 cm. B, within vagina in scar tissue.	6 mm. 6 mm.		0.5-1 mm.			Normal.	Fibrous tissue.	A, 1 layer cuboid or almost flat. B, 3 to 20 layers squamous ephithelium.		
2133	5846	33	"	1	"	0	2	Posterior wall close to scar in sulcus.	...	...				Normal over both.	Fibrous tissue.	A, lined by several layers of squamous epithelium. B, apparently lined by cuboid epithelium.	Desquamated epithelium. Mucus.	
2137	5850	39	"	1	"	0	1	Left vaginal fornix.	1 cm.		1.2 mm.			Thinned out over prominent part.	Fibrous tissue.	One layer cuboid epithelium.		
2555	6287	35	"	3	"	0	1	Right vaginal fornix to right of cervix.	1x1 5 cm.	Globular.	1 mm.	Clear fluid.	Smooth	Normal		One layer cylindric in places cuboid epithelium.		
2727	6504	29	"	5	"	0	..		5 mm.	Round.				...	Fibrous tissue.	Many layers squamous epithelium.	Partly filled with squamous epithelium.	
2878	Specimen.	..		..	..		.		1 cm.	Globular.	0.3 mm.			Normal but atrophic.	Fibrous tissue along one side gathered into little folds.	One layer cylindric epithelium.		
2890	6656	48	White.	1	Yes.	0	1	Right vaginal sulcus in scar.	1.5 cm.	...			Smooth	Normal.		One layer very low, cuboid epithelium almost flat.	Mucus taking hematoxylin stain.	
2930	6703	21	"	1	Complete.	0	2		2 mm. 1 mm.	Globular, side by side.			Smooth	Normal.	Just beneath cyst epithelium non-striped muscle fibres.	Each cyst lined by one layer cuboid epithelium.		
2981	6714	36	"	4	Yes.	0	..		Embed'd 2 mm. in scar tissue.	Oval.			...		Just beneath epithelium of cyst dense area containing giant cells, some with nuclei in center, others in periphery; centers of some contain a faintly granular mass.	3 to 8 layers flattened squamous epithelium.	Desquam. and necrotic epithelium and irregular masses of granular material similar to that found in the giant cells.	
3046	6787	40	"	6	"	0	..		6 mm.	Globular.	2 mm.			Normal.	Fibrous tissue.	1 to 15 layers of squamous epithelium.		
3089	6841	33	White.	1	Yes.	0	..	In right lateral wall.	1.4x1. 1 cm.	Globular.	1 mm.	..	Smooth.	Gathered up into folds; deep layer pigmented.	Fibrous tissue.	1 layer cuboid or flat epithelium.		
3107	6855	34	"	3	..		1	Left lateral wall just within hymen.	3x1.4 cm.	Oval.			Smooth.	Normal.	Just beneath cyst lining two small gland-like spaces lined by cylindric epithelium.	1 layer cuboid cells, apparently 2 to 3 layers in a few places.	Granular material taking hematoxylin stain.	Pearly white, covered on one side by squam. epithel.
3151	6887	38	"	4	Yes.	0	1	Posterior vaginal wall.	3x2 cm.					Normal but atrophied over prominent part.	Fibrous tissue.	3 to 20 layers of squamous cells.		
3321	7038	21	"	1	"	0	1	Left wall.	Cystic mass (of 3 cysts) 9 mm.		0.2 mm.		Somewhat irregular.	Normal.	Slight projections of fibrous tissue into cyst cavities; walls between cysts exceedingly delicate.	2 to 8 layers of squamous epithelium.		

ANALYSIS OF VAGINAL CYSTS OBSERVED AT THE JOHNS HOPKINS HOSPITAL DURING THE PERIOD 1893 TO JANUARY 1, 1904.—*Continued.*

Gyn. Path. No.	Clinical No.	Age.	White or Black.	Para.	Perineal tear.	Previous perineal operation.	No. of cysts.	Site of cysts.	Size.	Shape.	Thickness of cyst wall.	Cyst contents.	Inner surface of cyst.	Condition of overlying vaginal mucosa.	Composition of cyst wall.	Epithelial lining of cyst.	Cyst contents (microscopic).	Remarks.
3690	7453	32	"	2	"	0	..	Embedded in scar tissue.	1.5 mm.					Depression from vagina 4 mm. into depth lined by partly macerated squamous epithelium only separated from cyst by 6 rows of connective tissue cells.	Fibrous tissue.	1 to 7 layers fairly well-defined squamous epithelium.		Definite inclusive cyst.
3800	7547	34	"	1	"	0	1	Post. wall near outlet embedded in fibrous tissue.	5 mm.							1 to 20 layers squamous epithelium.		Desquam. epithelium, fine granular material.
4060	7804	35	"	4	"	0	1	Left lateral wall in scar.	3 mm.	Slightly irregular in outline					Dense fibrous tissue.	Apparently one layer of squamous cells.		
4079	7835	26	"	3	"	0	2		A, 4 mm. B, 3 mm.			A, yellow B, clear fluid.		Thinned out; groups of small round cells beneath surface epithelium.	Fibrous tissue; partition between cysts very delicate.	A, 1 to 4 layers of squamous cells. B, 1 layer cuboid cells.	A, desquamated epithelium + débris.	Interesting to find different kinds of cysts side by side.
4112	7854	37	"	10	..		..		2 mm.	Round.						2 to 20 or more layers squam. epith. cells stain more deeply than usual; a few polymorphonuclear leukocytes betw'n epithelial cells.		Double vaginal septum removed.
4644	8457	19	"	0	..		1	Anterior vaginal wall just within hymen.	3x3x4 cm.		1 mm.	Clear fluid.		Normal.	Fib. tissue; definite inner zone of non-striped muscle running parallel to cyst; beneath inner epithelium a definite stroma in places; cells are round or oval, have deeply staining nuclei, resemble stroma of uterine mucosa.	1 layer of cuboid or low cylindric epithelium clinging to inner surface.	A few mono- and polymorphonuclear leukocytes.	
4684	San.	..	"	Yes.	Yes.	0	..		3 mm.						Fibrous tissue.	2 to 7 layers of squamous cells.		
4836	8641	33	"	2	Complete.	0	..		5x2 mm.		2 mm.	. ..		Normal.	Fibrous tissue.	10 to 30 layers of squamous epithelium; superficial layers disintegrated.	Desquamated epithelium, débris, and large droplets, apparently fat.	
5035	8844	33	"	3	..		1	Ant. vaginal wall under urethra.	2.5x1.5 cm.	Ovoid.	0.2 mm.		Smooth.	Atrophic over prominence on sides thrown into long tongue-shaped folds.	Fibrous tissue, here and there infiltrated by clusters of small round cells.	1 layer of cuboid or almost flat cells.		
5037	8846	50	White.	3	Yes.	0	..		7x8 mm.					Normal.	Fibrous tissue.	1 layer of almost flat cells, cuboid type.		
5043	8851	38	"	3	"		..		3 mm.	Round.	2 mm.			Normal.	Fibrous tissue within blood vessels.	2 to 7 layers of squamous epithelium.		

ANALYSIS OF VAGINAL CYSTS OBSERVED AT THE JOHNS HOPKINS HOSPITAL DURING THE PERIOD 1893 TO JANUARY 1, 1904.—*Continued.*

Gyn. Path. No.	Clinical No.	Age.	White or Black.	Para.	Perineal tear.	Previous perineal operation.	No. of cysts.	Site of cysts.	Size.	Shape.	Thickness of cyst wall.	Cyst contents.	Inner surface of cyst.	Condition of overlying vaginal mucosa.	Composition of cyst wall.	Epithelial lining of cyst.	Cyst contents (microscopic).	Remarks.
5058	1194 San.	..	"	Yes.	Yes.		1	Posterior vaginal wall.	5 mm.	Round.	2 mm.		Smooth.	Normal.	Fibrous tissue.	3 to 8 layers of squamous epithelium.		
5191	9028	31	"	1	"		1	Posterior vaginal wall.	4 mm.							4 to 6 layers of squamous epithelium.	Filled with desquamated epithelium.	
5450	San.	..	"	Yes.	"		..	Posterior wall.						Normal.	Fibrous sissue.	2 to 4 layers ill-defined squamous epithelium.	Granular detritus.	
5509	9314	25	"	1	"		1	In left posterior wall embedded in deep scar.	8 mm.					Atrophic but normal.	Fibrous tissue.	2 to 10 layers of squamous epithelium.		
5593	San.	..	"	Yes.	Complete.		2		1 mm. 1.5 mm.	Round.		...		Normal.	Fibrous tissue; small circular clumps of epithelium; near center two definite glands lined by cylindric epithelium.	Many layers squamous epithelium; polymorphonuclear leukocytes between epithelial cells.	Filled with desquammated epithelium and polymorphonuclear leukocytes.	Definite inclusion cyst, also well-defined vaginal glands.
5792	9596	26	"	1	Complete.		..		5 mm.		1 mm.	Clear fluid.			Fibrous tissue.	Apparently cuboid or almost flat epithelium.		
5793	9595	28	"	2	Complete.		..		3 mm.	Round.		Yellow and opaque.			Fibrous tissue.	3 to 10 layers of squamous epithelium; superficial layers degenerated—contain large vacuoles.		
5819	9621	32	"	6	Complete.		..		1.5 mm.	Round.	3 mm.	Yellow and opaque.		Normal.	Fibrous tissue.	2 to 8 layers of squamous epithelium; superficial layers almost colorless; vacuolated.		
6274	Specimen.	..					..		1 cm.		1 mm.					Single layer columnar cells.		
6290	San.	..	White.	Yes.	Complete.		..	Lateral wall.	1 cm.		2 mm.	..	Smooth.	Normal.	Fibrous tissue; contains irregular gland-like spaces lined by very high cylindric epithelium secreting mucus; most of glands open into 1 cavity.	1 layer of high cylindric epithelium and a few gland-like spaces at irregular intervals just beneath cyst cavity.		May have developed from urethral glands or Skene's ducts.
6536	San.	..	"	Yes.	Yes.		..		1 cm.	Round.	2 mm.			Normal.	Fibrous tissue.	1 to 15 layers degenerated squamous epithelium.	Partially filled with desquamated epith. and crystals.	
2380	6118	35	"	2	"		1	Ant. vaginal wall under urethra.	3.5x2.5x2 cm.			Clear yellow.		Normal.		1 layer columnar or cuboid cells.		
2442	Specimen.	..		...			..							Normal.		1 layer columnar epithelium; oval nuclei near bottom of cell; protoplasm takes hematoxylin stain.		
2872	Specimen.	..					1		1x0.5 cm.	Oval.				Normal.	Fibrous tissue.	Remarkable picture 3-8 or 9 layers, the superfic. layer high cylindric resting on flattened deeply staining cells; the cylindric cells bear resemblance to cervical epithelium.		

THE ETIOLOGY AND PATHOGENESIS OF PERNICIOUS ANÆMIA.[1]

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The problem presented for solution by progressive pernicious anæmia is one of considerable difficulty, and to this difficulty there are many contributing factors. The general features of the disease offer scarcely a hint to one in search of the causal factor or factors. The malady is widely distributed geographically with few local variations in prevalence except that in Switzerland, and especially in the vicinity of Zürich, it is reported to occur more frequently than elsewhere, which may be due in part to the unusual interest in the disease which was aroused in that locality by the work of Biermer, Gusserow, and Eichhorst. On the other hand it is claimed that Munich and Prag enjoy a relative immunity. There is no racial peculiarity of distribution, and while most of the cases reported are from among the white races, as would be expected, in McCrae's series of 40 cases from Dr. Osler's wards at the Johns Hopkins Hospital, there are two negroes.

As to sex, there is some disagreement in statistics. In Germany it is commonly taught that there is a greater prevalence among women, an assertion which is based on such series as those of Ehrlich, showing 130 women to 110 men, and of Lazarus, from the Berlin hospitals, of 172 women to 102 men. In England and in the United States, with perhaps more rigid criteria of diagnosis, the majority of the cases are in the male sex. Of Cabot's 50 cases, 33 were males; of McCrae's 40, 32 were males; Hunter reports 19 cases in men, 6 in women, and Colman reports in a series of cases, analyzed by him, 60 males and 27 females. From the tabulation of a number of series of reported cases Colman found 323 males and 227 females, and calls attention to the fact that while in earlier statistics women predominate, in the later, men are decidedly more numerous.

Though affecting people at the extremes of life, the disease is of the greatest frequency in those of middle age. The majority of Lazarus' cases fell in the third and fourth decades. McCrae and Cabot find the disease is most frequent in the fifth decade; Colman, between the 35th and 45th years. Monti and Berggrün have collected from literature 16 cases under 15 years of age, and both Cabot and Lazarus report two cases in the eighth decade.

The patients affected are said to be more often of the robust habit than otherwise. Occupation seems to bear no causal relation, nor mode of life. Although the earlier opinion seems to have been that pernicious anæmia was chiefly a disease of the poorer classes, the later view, as expressed by Lazarus, is that the proportion of cases among the well-to-do is above the ratio of the well-to-do to the poorer class. In a few cases a family tendency to the disease is suggested.

In a search for more immediate causes, one is confronted by another difficulty in the very nature of the disease. One is dealing with a chronic disease and one of so insidious an onset that the patient comes to the attention of the physician only when the process is well advanced and the patient himself is unable to tell definitely when it began, and what were the contributing causes. A good percentage of cases can give a history of no contributing factors, but a large number of severe, progressive, and fatal anæmias have followed events or have been associated with lesions well recognized as giving rise to anæmias of a secondary type. This has raised the question as to whether these lesions are to be considered as causal factors of the pernicious anæmia or as associated conditions; and if they be accepted as the causal factors, are we to group together the whole series, those anæmias with apparent causes and those without, as representing a symptom complex, a clinical picture presented by all serious anæmias, or are we to separate the anæmias without apparent adequate cause from the other group, as a distinct clinical entity? The question is as old as the two classical descriptions of the disease, that of Addison, published in his monograph on Disease of the Suprarenal Capsules in 1855, and that of Biermer, published in 1872; and one can perhaps best arrive at our present conception by reference to those two papers.

Addison described a "very remarkable form of general anæmia occurring without any discoverable cause whatever; cases in which there had been no previous loss of blood, no exhausting diarrhœa, no chlorosis, no purpura, no renal, splenic or miasmic, glandular, strumous, or malignant disease. Accordingly in speaking of this form in clinical lectures, I perhaps with little propriety applied to it the term 'idiopathic' to distinguish it from the cases in which there existed more or less evidence of some of the usual causes or concomitants of the anæmic state. The disease presented in every instance the same general character, pursued a similar course, and with scarcely a single exception was followed after a variable period by the same fatal result. It occurs in both sexes, generally, but not exclusively beyond the middle period of life, and so far as I at present know, chiefly in persons of a somewhat bulky frame and with a strongly marked tendency to the formation of fat. . . . On examining the bodies of such patients after death, I have failed to discover any organic lesion that could properly or reasonably be assigned as an adequate cause of such serious consequences."

Biermer in 1872 reported 15 cases of anæmia occurring between the ages of 18 and 52 years with the symptoms of a

[1] Paper read before the Medical and Chirurgical Faculty of Maryland, December 16, 1904.

progressive pernicious anæmia, and which he concluded were caused by insufficient and unsuitable nourishment, unhygienic dwellings, exhausting discharges, in particular long-continued diarrhœa, and also, at times, by diseases accompanied by hæmorrhages, including in a common group anæmias with these causal factors and those with undiscovered cause.

These two views express practically the division that exists to-day among the clinicians on the subject, the Germans adhering to the Biermer view, while the English and American authorities are inclined to accept Addison's. It would lead too far afield to quote fully the expressions of opinion on the matter. Let two quotations suffice.

William Hunter, possibly an extremist on the one side, maintains: "The anæmia which Addison described is really a remarkable infective disease with definite antecedents, mode of origin, infective and hæmolytic lesions and clinical course. On the other hand, the investigations which have made this clear have also made clear that the condition described by Biermer is as its supporters truly maintain 'not a disease *sui generis,* but a frequently recurring group of symptoms met with in very different conditions of disease,' 'not an etiological unity, but only a symptomatic group which can be produced by causes of all kinds'; the most common cause being, as I hope to show, septic infection, this being the feature that has led them to be confounded with Addison's Anæmia."

On the other hand, Grawitz, among others, maintains that "the etiology of the symptom picture of pernicious anæmia is not uniform, many influences playing a part," and "the diseases showing this symptom-picture bear even as little relation to each other as do the members of other groups of diseases which have, as a striking feature, albuminuria or glycosuria."

The pathological conditions which have been regarded as bearing a causal relation to severe progressive anæmias is an extensive one. It includes, according to Stockman:

Pregnancy (Gusserow and many others).

Severe or protracted hæmorrhages (Habershon, Quincke, Schepelern, Finny, Greenhow, Stockman).

Gastric atrophy (Fenwick, Brabazon, Nothnagel, Henry, and Osler).

Typhoid fever (Rosenstein).

Syphilis (Mueller, Laache).

Yellow fever (Bramwell).

Mental shock (Mackenzie, Cortin).

Chlorosis (Mueller, Hall, Coupland).

Malnutrition.

Jaundice.

Sarcoma and carcinoma involving the marrow (Mosler and Gast, Grawitz).

Carcinoma of stomach (Nothnagel, Eisenlohr).

Intestinal parasites—Ankylostoma and Bothriocephalus (Schauman, Sahli, Leichtenstern).

These are all conditions, which if associated with anæmia, are, in the great majority of cases, accompanied by an anæmia of the secondary or chlorotic type. It seems probable in some of the reported cases that severe anæmias of the secondary type have been diagnosed progressive pernicious anæmia. For example, as to the causal part played by pregnancy, Lazarus notes that in recent years far fewer cases of pernicious anæmia following pregnancy are reported than in earlier years before the criteria for the diagnosis of pernicious anæmia were well established. He quotes Ahlfeld to the effect that he has never seen a case following pregnancy in his obstetrical practice. Such is also the experience of J. Whitridge Williams.[2] This may account for the change in the ratio of sexes affected, already noted as shown by Colman's statistics. Granting however, as one must, the occasional occurrence of these two conditions in the same patient, are we to ascribe to pregnancy a causal relation? In a chronic disease, which, when well established, may extend over three or four years of the patient's life during the child-bearing period, is it not more rational to look at the association of the two conditions as a coincidence,—the occurrence of a physiological event during the unrecognized state of anæmia? Or where causal relation seems indisputable, must not one look for some other factor to explain why this normal event in a woman's life should very exceptionally be followed by pernicious anæmia? In this light the improvement in obstetrical technique and the lessened number of cases of puerperal infection may account for the diminution in the number of cases of anæmia following pregnancy noted by Lazarus and others, and if such prove the case, it would tend to confirm Hunter's theory as to the real causal factor in such cases.

Certain of these arguments seem applicable to other conditions mentioned. Few would accept, for example, the case reported by Stockman following hæmorrhage, in which the red-blood corpuscles were reduced to one-fifth their normal number and the hæmoglobin to one-tenth its normal percentage, as giving the blood picture of pernicious anæmia—but rather as showing a severe secondary anæmia.

Jaundice is clearly to be regarded as a symptom, not a cause.

Gastric atrophy seems to occupy a different relation to pernicious anæmia than the conditions just discussed. Only a small percentage of cases of achylia gastrica and gastric atrophy present the picture of pernicious anæmia. A considerable number of cases of pernicious anæmia show gastric lesions which may be considered as early stages of a chronic inflammation, the result of which would be gastric atrophy. Some cases show complete atrophy of the gastric mucosa. Under such conditions one is not justified in ascribing a causal rôle either to the anæmia or to the gastric lesion. In some cases the symptoms of the gastric atrophy manifest themselves before the anæmia, in others not until considerably afterward, in still others, practically simultaneously, a time relation quite similar, as is noted by Faber and Bloch, to that presented by the spinal cord symptoms in pernicious anæmia; and the opinion of these authorities and of the majority of

[2] Personal communication.

recent writers on the subject is, that one must look at the blood lesion, the gastric lesion, and the cord lesion, as due to a common cause, and thus all features of the disease, pernicious anæmia.

The parasite Ankylostoma (Uncinaria) is generally assumed to produce an anæmia by abstracting blood from the intestinal walls, and in the great majority of cases it produces an anæmia of the secondary type. Thus Rogers in 1900, in reporting on uncinariasis in Assam, quotes Sandwith of Cairo, as reporting "in 173 cases of Ankylostomiasis, the percentage of hæmoglobin to be reduced nearly twice as much as that of the red-blood cells so that the color index was reduced to about one-half, just as it was in my own (Rogers) cases, allowing for the abnormally low hæmoglobin-value of healthy Assamese." It seems probable then that in cases where the picture of pernicious anæmia follows infection with these parasites, some further factor is to be sought.

Bothriocephalus latus, on the other hand produces an anæmia which is accepted by Lazarus, among others, as a pure picture of pernicious anæmia, and the parasite is regarded by him as the only positively recognized cause of the condition. The experiments of Schaumann and Talquist have shown that a substance may be extracted from the worms which is actively hæmolytic and this has led to some theorizing as to the pathogenesis of pernicious anæmia, to be referred to later.

Although some of the severe anæmias in literature may thus be excluded from the pernicious anæmia group, by rigid application of the diagnostic criteria—and although some supposed causal factors are apparently associated lesions, there are still cases following conditions, the well-recognized causes of secondary anæmias, which present the picture of pernicious anæmia. As to these in the present state of our knowledge of pernicious anæmia it seems impossible to say whether we are to assume that in some stage, any severe secondary anæmia may give the picture of pernicious anæmia or whether we may expect to find a common, as yet undiscovered cause for both the "idiopathic" group and the "symptomatic." However that question may be decided, one seems justified in assuming that the so-called "idiopathic" cases which show such uniform symptoms and blood findings, so similar a course and termination are entitled to a position as a clinical entity and that one may hope to find for them a single cause—and this disease we may define in Cabot's words, with a slight modification, as a profound and almost invariably fatal anæmia without adequate known cause, characterized by an extreme diminution in the number of red-blood cells and usually by other changes in the blood, indicative of a pathological mode of blood formation, as well as absence of emaciation and a tendency to spontaneous temporary improvement followed by relapse.

This position is arrived at, however, from a clinical rather than from a pathological standpoint. The pathological picture is, in general, one that might be expected as a result of a profound anæmia. The common findings are a lemon-tinted skin, well preserved adipose tissue, often of a brilliant yellow color; bright-red muscles; as a rule, an excessive amount of usually fluid, watery blood with soft clots; a serum which may have a tint as if bile-stained; extreme anæmia of all organs; marked fatty degeneration of the heart; frequently general petechial, subserous, submucous, and retinal hæmorrhages; a spleen of variable size, seldom very large; prominent hæmolymph glands; a pigmented kidney. The fatty marrow of the long bones is usually replaced by a greyish-pink or red, rather firm marrow; but exceptionally the fatty marrow persists and even replaces the red marrow of the cancellous bone near the epiphyses and in the ribs.

The microscopical examination adds little save that it shows in the spleen, and especially in the epithelial cells of the liver and kidneys, an excess of fine, yellowish granules which give the reaction for free iron. In the liver this pigment is pretty generally distributed in the lobule, but most heavily toward the periphery, where it is arranged in the cells in rows, surrounding the bile capillaries. In the kidney it lies in the tubules of the secreting type, perhaps especially in the ascending loops of Henle.

The marrow shows a picture not usually seen in actively regenerating marrow. One misses the preponderance of erythrocytes and normoblasts usually present and finds, instead, that the more frequent cell of the erythroblastic group is of the megaloblastic type. This was noted first by Cohnheim who called attention to its resemblance to embryonic marrow and suggested that it might be considered a reversion of the marrow to the youthful or embryonic type. Ehrlich designates the condition a "metaplasia."

In a certain percentage of cases, there are also spinal cord lesions, consisting of bilateral and usually symmetrical areas of degeneration and sclerosis confined chiefly to the posterior columns and the postero-lateral region, and in other cases, foci of degeneration about small vessels. There seems to be some question here, as to whether the more extensive changes are to be considered as a system disease, or as the result of the fusion of the focal lesions.

Likewise, in many cases there are demonstrable in the mucosa of the stomach lesions of a chronic type, varying from fatty degeneration of the tubules with increased, small, round-cell infiltration of the interstitial tissue to complete atrophy and sclerosis of the mucous membrane. Hunter calls attention to further lesions of an infectious type in the gastro-intestinal tract, in particular, a deep-seated inflammation of the tongue.

Such, in brief, are the general etiological factors and pathological findings. How are they to be interpreted in an effort to ascertain the cause and the pathogenesis of the disease?

In the first place it does not seem necessary to assume any specific predisposition to anæmia—at least not a predisposition with a pathological condition of the marrow as a basis. There is, however, a disproportion between the resisting power of the individual and the strength of the pathological agent producing the anæmic state—a disproportion shown by an

inability of the bone marrow to generate a sufficient number of red-blood cells to supply the deficiency. This disproportion is especially marked in the so-called "aplastic" cases, in which after death the marrow is found to be fatty and with practically no sign of regeneration. Whether this variability in reaction depends entirely on a variation in the intensity of the toxic agent or in part on the condition of the individual is the same problem as is presented in many diseases, as for example the variable resistance offered to invasion by the tubercle bacillus, or to the toxic agents producing a nephritis or a cirrhosis of the liver. It would seem to depend more on a general lack of resistance on the part of the individual than to any special predisposition or weakness of the bone marrow.

It is obvious that an anæmia may be produced in several ways: First, by insufficient or defective blood formation; second, by excessive loss of red-blood cells from the circulation, third, by excessive destruction of red cells; or, fourth, by a combination of the preceding factors or any two of them.

The picture of pernicious anæmia gives some evidence of the operation of each of these factors, and it is according to the emphasis placed on any one, that one must group the attempted explanations of the pathogenesis of the disease. It is not possible to give fully all of the theories as to causation in this paper, and a few selections must suffice.

Since Cohnheim in 1876 noted the hyperplastic condition of the bone marrow and especially the presence of the large, nucleated red cells of the megaloblastic type, and more especially since Ehrlich in 1880 called attention to the presence of the megalocytes and megaloblasts in the blood, the cause of the disease has been sought in the marrow, and there is a considerable group of supporters of the theory that this reversion of the bone marrow to an embryonic type is the primary lesion. Such was Cohnheim's idea.

In a recent paper Bloch adheres closely to this view, expressing the opinion that "Biermer's anæmia rests almost always on an asthenic condition of the hæmopoietic system, usually congenital, as a result of which the red-blood cells are insufficient for their function, or of a more unstable structure (chemical and physical), and therefore less resistant to injurious agents. All causal factors, to which the disease is often ascribed, are to be considered simply as accidental, exciting causes. It is a chronic disease, or better expressed, the establishment of the clinical picture, of which the characteristic lesion is a transformation of the bone marrow into a megaloblastic, embryonic type, requires a long time."

Houston says: "The changes found in the bone marrow in cases of progressive anæmia are an essential lesion of the disease directly accounting for the condition of the blood, and not, as some have supposed, of a secondary nature, the result of a severe anæmia."

Grawitz is probably to be included in this group as he recognizes two factors in pernicious anæmia, an individual predisposition and a pathological method of hæmopoiesis, his contention being that "the principal difference between pernicious and other severe anæmias lies not so much in the blood findings or not so much in the differences in the etiological moment as in the clinical course, the characteristic being that the progress of the anæmia is not checked, after removal of the cause, by a regenerative process in the hæmopoietic organs, but that after the removal of the cause, the blood formation proceeds in a faulty manner, producing an insufficient number of pathological cells."

William Pepper believed also in a deficiency in blood formation, designating the condition an "anæmatosis."

Stockman is the only recent writer who lays great stress on the part played by hæmorrhages in pernicious anæmia, yet, as has been previously noted, I think one must disagree somewhat with his interpretation of what constitutes the blood picture of anæmia, as well as with his dictum that pernicious anæmia is "simply a collection of symptoms characteristic of the highest degree of anæmia." He holds, as to the pathogenesis of the condition, that it is due to the following factors:

First, it follows on well-recognized debilitating causes.

Second, degenerative changes take place in the whole vascular system and these permit the occurrence of

Third, minute capillary internal bleedings, more rarely of external ones also, and that a persistent continuance of these leads ultimately to excessive anæmia and death.

Since the discovery by Quincke in 1877 of the excessive amount of iron in the liver of pernicious anæmia patients, its confirmation by Peters, and by the careful analyses of Hunter, together with the finding of iron-containing pigment in the kidney, and the determination of an excessive excretion of hydrobilirubin by the kidneys, an excess shown to increase during the exacerbations of the disease, diminishing again during periods of improvement (Hunter), as well as the determination of hæmoglobin and hydrobilirubin in the plasma of the circulating blood (Syllaba), sufficient evidence seems to have collected to show that if not the essential process, at least a major factor in the disease is the destruction of red-blood cells, a hæmolysis. There is no stronger advocate of this theory than William Hunter, who has also gone further than others in outlining a theory of the causation of the disease. He points out that in analyses of seven cases of pernicious anæmia, the liver and kidney contained 360 milligrams of iron per 100 gm. of dried organ substance, and the spleen, but 125 milligrams, while in seven cases of secondary anæmia, the spleen contained 362 milligrams and the liver and kidneys but 79. He lays great stress on this reversal of conditions in the two varieties of anæmias, and interprets it as indicating an excessive destruction of red-blood cells occurring in the field of the portal circulation and due to a toxin elaborated in the intestine. In 227 out of 273 cases of pernicious anæmia, or 83%, there were severe gastro-intestinal symptoms. Pathologically in a large percentage of his own cases, he records the presence of infective lesions in the gastro-intestinal tract either a "glossitis" of specific char-

acter or other forms of oral, gastric, or intestinal sepsis. As a result he concludes pernicious anæmia is a chronic infectious disease localized in the alimentary tract, caused by a definite infection of certain of its parts, chiefly of the stomach, occasionally also of the mouth and intestine. It is characterized by intermittent destruction of red-blood cells, by periodic disturbance of the alimentary tract, by occasional toxæmic attacks characterized by fever, sweats, and general nervous symptoms. Hunter's theory disregards the alterations in the bone marrow which are seen in pernicious anæmia, and it seems to fall short of a complete explanation not only in that respect, but also in this that, while he does not consider hæmorrhage to be a causal factor in the production of the disease, he does lay great stress upon the causal relation of a destruction of red cells in one field of the circulation—which to the whole system is but the equivalent of an internal hæmorrhage.

The Ehrlich-Lazarus theory recognizes the probability of the presence of some hæmolytic substance, calling attention to the bothriocephalus anæmias in which it has been shown that a hæmolytic substance is produced by the parasite. They assert that it is not necessary to assume a pre-existing abnormal marrow, but that all anæmia-producing influences stimulate the marrow to hyperplasia; that too long or too intense stimulation leads to the production of a megaloblastic marrow; that the capability of the marrow to react to stimulation is limited. Moreover, the difference in reaction between the normoblastic type of marrow and the megaloblastic may rest on a qualitative rather than a quantitative difference in stimuli—that there are stimuli of moderate intensity, but of special character which may cause the megaloblastic reaction as in bothriocephalus disease. They conclude that the anomaly of blood formation and the increased blood destruction are coördinate results of the same cause. "This cause," says Lazarus, "inasmuch as we have no other explanation for the megaloblastic transformation of the marrow than the presence of some toxic substance, we will assume to be the formation of toxins which have the capability of influencing the marrow in this specific manner."

To the mind of the writer, this latter theory approaches most closely the true solution of the question of pathogenesis—that of the absorption of a toxic substance, probably of intestinal origin, which acts on the circulating blood producing hæmolysis and through the circulation also on the marrow, resulting in a faulty hyperplasia. That this toxin is a result of gastro-intestinal infection as suggested by Hunter seems not improbable. There are other evidences of a toxic substance circulating in the blood—notably, the symmetrical lesions found at times in the spinal cord, which practically all investigators agree are the result of a toxin, and not of the anæmia *per se* as they are not found in even the severest types of secondary anæmia. According to Minnich, they resemble the lesions of Ergotism, Pellagra, and Lathyrismus. The atrophy and degeneration of the gastric tubules may possibly be atributed to the action of a circulating poison, if not due to an inflammatory process. Finally, in the multiple capillary hæmorrhages, quite resembling the hæmorrhages with such intoxications as those due to snake venoms where they are, according to Flexner, the result of an endotheliolytic principle or "hæmorrhagin," one has evidence of further toxic action.

This leaves unsettled the question of the nature of the toxin and of its mode of action on the bone marrow to produce its effect. While the writer recognizes the danger of drawing conclusions as to human pathology from animal experimentation and observation, certain findings in such experimental work seems to indicate a possible answer to the question. While studying the effects of artificial myelotoxic sera on the bone marrow of rabbits, the author became convinced that the statement of Ehrlich that megaloblasts are not a normal constituent of the adult bone marrow is an error, at least as far as the rabbit is concerned. Further search showed cells of the megaloblastic type in the marrow of all the common laboratory animals as well as in human marrow—a finding in agreement with the views of Engel, Pappenheim, and others. From this study it seemed certain, also, that there was a definite arrangement of both the leucocytic and erythrocytic cells of the marrow in nests and groups, and of the erythrogenetic groups, as expressed at that time,[3] the megaloblasts formed the proliferating center, corresponding to the position held by the myelocytes in the leucogenetic centers. Peripherally to the megaloblasts were found nucleated red cells of a smaller type, but with vesicular nuclei; with these and outside, normoblasts with pyknotic nuclei, and, at the extreme periphery mature red cells. In actively regenerating marrows mitotic figures were frequent in cells of the megaloblast size and type, and were occasionally found in smaller cells of the intermediate type. The normal mode of development of the red cell, then, seems to be as follows: A division of the megaloblastic cell produces either its like or a smaller cell, that called by the clinicians the "intermediate" nucleated red corpuscle. By reproduction of these, the normoblast results, while by a still further change, the absorption of the pyknotic nucleus, the mature non-nucleated red cell develops. This differs in no essential, except as to the fate of the nucleus, from the description given by Howell of the process of blood formation in the cat. This theory assumes that the division of the megaloblasts gives rise to cells differing in size and slightly in type from their ancestors—a condition paralleled probably in the lymph glands where in cases of hyperplasia, mitoses are found most numerously in the large cells of the germinative center. Outside of the hæmopoietic system, a similar process is seen in the tubules of the testicle, where the outer cells or spermatogonia differ from their descendants, the spermatocysts, and these again from the products of their division, the spermatoblasts.

As a result of this grouping of the erythrogenetic cells, the older and more mature red cells are constantly pushed toward the periphery by the division of the cells at the center, and

[3] Univ. of Penn. Med. Bulletin, July, Aug., 1903.

thus the non-nucleated red cell comes to lie farthest away and nearest the capillaries. In like manner it may be observed that the polymorphonuclear cells occupy the periphery of the leucogenetic groups lying nearest the capillary wall; and thus it is that on stimulation the marrow is able to respond with mature red and white cells.

More recent experiments show that the reaction of the marrow to different stimuli differs, depending upon whether the stimulus acts on the red cells of the circulation as in the case of a hæmorrhage or its equivalent, the destruction of red corpuscles in the peripheral vessels or upon the marrow itself as in the presence of a circulating toxin.

Let me quote one experiment illustrative of the reaction of the marrow to hæmorrhage and the blood picture resulting: A rabbit was bled from the ear-veins daily with a few exceptions for 18 days, the daily amount of blood extracted varying from 2-20 cc., the total amount being 184 cc., an average of practically 10 cc. per day. Daily complete and differential counts of the blood were made just before each bleeding and on one occasion, two hours afterward. As a result of the hæmorrhages the red corpuscles were reduced from a total of 5,988,000 cells per cu. mm. on the first day to 2,486,000 on the 19th day when the animal was killed. In none of the counts 24 hours after bleeding was there found a large number of nucleated cells; the highest number was 16 cells of the normoblastic type to the cu. mm. In the count two hours after the bleeding 108 normoblasts were found per cu. mm., the percentage being estimated from the number of such cells seen while counting 500 leucocytes, a method of approximate accuracy. Postmortem, the marrow showed the usual hyperplastic picture—the normoblasts being the predominant nucleated red cells.

In another rabbit, where 45 cc. of blood were taken at one bleeding and 27 cc. on the next day, the red count being reduced from about 7,000,000 to 2,592,000, there were as few nucleated red cells seen as in the previous case,—but 12 normoblasts per cu. mm. the first day and none the second.

Experiments with myelotoxic and hæmolytic sera give an entirely different reaction. In one dog which received intravenously 3.5 cc. of serum of a rabbit immunized against dog's red corpuscles, there were present in the circulating blood 24 hours later 900 nucleated red cells of the normoblastic type and 120 of the megaloblastic variety; at the end of 48 hours the number was approximately the same, the normoblasts numbering 928, and the megaloblasts 64; at 72 hours there were 500 normoblasts and no megaloblasts. The animal was not followed further.

On account of greater ease in manipulating and standardizing the toxin, the later experiments have been performed with ricin, a soluble toxalbumin from the castor oil bean, which has marked toxic action for leucocytes and red-blood cells in the rabbit. The hæmolytic action is shown by numerical reduction in red cells, by hæmoglobinuria and by deposits of pigment in spleen and lymph glands. The blood picture is quite uniform. One animal which had received a lethal dose of ricin intravenously showed, 24 hours afterward, 1130 normoblasts, 603 naked pyknotic red-cell nuclei, and 335 megaloblasts per cu. mm.

A second animal which had received a smaller dose showed, a day later, 1120 normoblasts and 875 naked red-cell nuclei, but no megaloblasts, with a reduction of 1,500,000 cells per cu. mm. in the total red count. On repeating the dose and waiting 8 hours, there were found 3472 normoblasts, 2884 naked nuclei, and 400 megaloblasts per cu. mm. The animal died during the second day.

Following smaller doses, and becoming marked when, after the reduction in red cells, the regeneration begins, the blood picture is quite suggestive of that seen in the pernicious anæmia. There are scattered nucleated red cells, the non-nucleated corpuscles show great variation in size, large cells or macrocytes being numerous; there is a slight tendency to poikilocytosis. After lethal doses the marrow itself gives direct evidence of the effect of the toxin in the presence of cells with pyknotic and fragmented nuclei and in minute hæmorrhages.

The conclusions I would draw from these experiments, which are still in progress, is that in hæmorrhage there is created a deficiency in circulating red cells, which is met by the marrow with the mature red cells lying close to the capillaries at the periphery of the erythrogenetic groups. In large hæmorrhages with exhaustion of the supply of mature red cells a certain number of normoblasts are called out to supply the deficiency.

On the other hand, with a circulating toxin, there is destruction not only of red cells in the circulation, but also of some, at least, in the marrow, even of normoblasts as suggested by the large number of naked nuclei found later in the circulation. The marrow responds, in this emergency, with nucleated red cells of normoblastic or megaloblastic type, depending upon the extent of the destruction. The experiment of the repeated dose of ricin where megaloblasts appeared only after the second dose would seem to confirm this idea, as well as the observations as to the arrangement of the cells in the erythrogenetic groups in the marrow.

Applying these conclusions to pernicious anæmia, it seems possible that an analagous toxin may be present, destroying red cells both in the circulation and in the marrow so that in the reaction, nucleated red cells are used to supply the deficiency—that further action of the toxin reduces the erythrogenetic groups more or less to the megaloblastic centers, diminishing greatly the regenerating power of the marrow and resulting in a discharge of megaloblastic cells in the hasty effort to supply the needs of the circulation. Thus, the regular orderly development of the groups of the marrow cells is interfered with and a short cut is taken from the megaloblast to the macrocyte, an imperfect, immature cell, as shown by its polychromatophilia and granular basophilia. In this light it is not difficult to see why cases of pernicious anæmia with few normoblasts, and more megaloblasts in the circulation are of graver prognosis than those with a large number

of normoblasts, and few megaloblasts. And again if one regard the presence of nucleated cells in the circulation as evidence of injury to the bone marrow, one has an explanation for the "nucleated red cells crises" of pernicious anæmia and leukæmia in which the blood picture resembles much that shown in ricin intoxication.

These observations and deductions seem to the writer to offer a not unsatisfactory explanation of the so-called reversion of the marrow to the embryonic type in pernicious anæmia.

Indebtedness is acknowledged to the following articles:

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RECURRING PHLEBITIS OF OBSCURE ORIGIN.

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There is a variety of phlebitis, affecting the veins of the extremities, and occurring in the absence of all conditions that are commonly recognized as predisposing to inflammation of the veins, which has attracted little or no attention from systematic writers. The cases, though apparently rare, are so similar in the essentials of their clinical course, and show so many striking and constant features in common, that they deserve for the present at least to be put together in a group by themselves, and to be sharply separated from other forms of acute venous inflammation. Clinically characterized by a progressive and relapsing course, they are obscure alike in their pathology and in their remote and immediate etiology. So consistent is the clinical picture which they present, that we may fairly consider them all, in our ignorance as to their more intimate nature, under the title of *idiopathic recurrent thrombo-phlebitis.* It is not asserted that the symptom-complex is a new one, for every one will recognize in the cases to be reported the main features emphasized by Paget, Prescott, Hewett, Tuckwell, Lancereaux, and others, as characteristic of the phlebitis associated with gout. But the present cases seem on the most careful consideration to be as certainly not dependent on this dyscrasia, as they are free from suspicion of a septic or traumatic origin. They are as remarkable for their apparent spontaneity as they are for the practical identity of their clinical details. It may be that we are not dealing with a new clinical group—it is even highly probable that we may be able eventually to refer these apparently mysterious cases to a variety of different causes. All that I shall attempt to show is that there occur cases of thrombo-phlebitis, with very individual and constant symptomatic features, yet differing from other forms of the affection, and with causes as yet absolutely unknown.

Case I. *Spontaneous thrombosis of the left internal saphenous vein* in a young man twenty-three years old. F. H. clear of gout and rheumatism, or other dyscrasia. Perhaps an unusually large proportion of his ancestors died of arteriosclerotic causes—cerebral hæmorrhage, interstitial nephritis, angina pectoris. Otherwise negative. P. H. Always healthy and active. Had the usual diseases of childhood. Lobar pneumonia at twelve years. Typhoid fever (?) at fifteen years. No venereal history. No migraines, dyspepsias, or other manifestations of the lithæmic diathesis. Acute follicular tonsillitis one year before the P. I., otherwise no acute infections other than an occasional coryza or laryngitis, during the eight years preceding it. Health unusually good at the time of onset, not leading a very sedentary life, though a student, and not doing any heavy muscular work nor liable to exposure.

P. I. In the latter part of May, 1901, the patient woke one morning with a sensation of stiffness at the inner side of the left ankle. This sensation disappeared during the day, to reappear the next morning with increased severity. On

the fourth day after this was first noticed, the front of the inner malleolus was found to be very tender on pressure. Examination showed that there was a firm and very tender cord running over that region, movable between the skin and the bone, and the veins of the lower extremity being rather large in caliber, it was possible by a comparison with the unaffected ankle to make sure that the cord was the obliterated internal saphenous vein in the lower part of its course. There was slight superficial redness and very slight œdema, confined to the malleolar region. Spontaneous pain was not marked, but walking was difficult, and there was some lameness for the next ten days or two weeks. At the end of this time the acute symptoms had subsided, tenderness had disappeared, and nothing remained but the tough cord, about 3 cm. in length, in the situation described. Careful and repeated examination of the foot and leg, and of the whole body, failed to reveal any, even the slightest, local infectious process; Hb. was 110%, and the general health, as always, excellent. The patient went on taking regular but not excessive exercise, and thought little of the incident.

Early in July of the same year the patient seemed to be wakened in the morning by a sharp, burning, almost intolerable pain in the left ankle and lower leg, and found that there was a thrombotic cord, continuous with the first one, extending some six inches above it along the inner side of the leg, and corresponding to the course of the saphena magna. There was already considerable œdema, confined to the inner half of the leg and ankle, not extending to the foot. There was some superficial reddening, not limited to the line of the vessel, and the surface temperature was higher than on the unaffected side. Tenderness was extreme. Prolonged immersion in a stream of cold water was effected several times a day, with the result of moderating the pain, and enabling the patient to walk about. The affection did not, at this time, progress further up the vein; the pain, heat, swelling, and tenderness gradually disappeared. At the end of two weeks the leg was again in normal condition subjectively, and showed on examination nothing but the characteristic firm cord at the site of the obliterated vessel. General health continued unimpaired, even when the pain was greatest; there was never any elevation of body temperature, and the leucocytes, counted twice during the acute stage, were below 8000 per cu. mm. One subjective feature of considerable interest at this time was that on waking in the morning pain was always intense, and it was often necessary for the patient to hop to the bathroom, when the cold water running over the leg for fifteen minutes would make it possible for him to put the left leg to the ground without agony. During the morning, in walking about, the pain would grow constantly less, returning to some extent always after sitting for any length of time; but by the middle of the afternoon it was usually possible for the patient to play a game of tennis without consciousness of pain or fatigue. This pain, after the leg had remained long at rest, growing less the more the limb was exercised, was a very characteristic feature during all the acute exacerbations, and suggested the existence of a certain degree of periphlebitis.

During the summer and autumn the patient suffered from three more acute attacks—one about August 15, affecting the vein as high up as the knee, the next in the early part of October, obliterating the saphena to a point 5 cm. above the knee, and the final one just before Christmas, continuing the process up to within a few cm. of Poupart's ligament in the thigh. In onset and course all the attacks were precisely similar to those already described. General health continued excellent, there was no exposure nor injury nor strain of the leg, and the patient suffered from no infections. The onset was always during the night, there was never any premonitory symptom, such as tenderness of the unobstructed portion of the vein or sense of muscular constraint, before the onset of thrombosis, and the attack was always definitely limited from the beginning. That is, after acute symptoms had once appeared and a cord had been made out continuous with the old one already present, this new cord never extended during the same attack beyond its upper limit at the time of its appearance. During none of the later attacks was the body temperature found to be over 98.8°, and on one or two occasions inflammatory leucocytosis was determined to be absent, and Hb. 100% or above. Disability was great during these later recrudescences, especially when the vein became involved at the knee, and for two days at this time the patient was obliged to keep to the house. Œdema was never very marked, appearing only in the inner half of the leg and in the segment corresponding to the inflamed vein, never extending beyond the median line in front or behind, nor affecting the leg at all below the point of blocking. This absence of mechanical œdema was accounted for by the fact of the patient having very large and numerous veins in the extremities, with abundant superficial anastomoses. But neither then nor since has there been any indication of a varicose condition.

Looking back on this case, especially in the light of the facts to be mentioned later, is enough to fill one with wonder that such contemptuous disregard of the embolic possibilities of the situation did not meet with its appropriate punishment. Absolutely no treatment was carried out, except the local application of cold, and this solely to relieve pain. The patient even walked about recklessly when the suffering was quite severe and the local inflammatory signs were at their height.

This case is reported in some detail, because it is quite typical of all, and may have an added value from circumstances which made its exact and continued observation possible. During the last acute attack the patient consulted Dr. McCrae at the Johns Hopkins Hospital, and he agreed perfectly in the obvious diagnosis. The case is also of interest as one of thrombosis of a large vein successfully treated without local rest, and perhaps illustrates the extreme of what a thrombus may undergo in the way of mechanical disturbance without dislodgement and the production of embolism.

At the present time, three years after the last acute attack,

the obliterated fibrous cord of the left internal saphenous vein can still be traced up to the middle of the thigh. The vein is quite impervious. Collateral circulation evidently is perfect, and there is and has been no œdema. Sometimes when fatigued after long walking or after exposure, there is a sense of discomfort complained of in the affected leg, a feeling of tension, or as of being conscious of the presence of the cord. Otherwise there have been no local sequelæ.[1]

The patient has been under constant observation. His general health has continued vigorous, and there have been absolutely no symptoms which the most fantastic could attribute to the existence of the lithæmic diathesis.

Case II. Patient aged about 40 years. F. H. unimportant—no gout or rheumatism. P. H. unimportant; lues doubtful. For three years has suffered from Raynaud's disease, and has fairly extensive necrosis of digits of all four extremities. Over the site of the left internal saphenous vein is a line of brown pigmentation in the skin, extending from the inner malleolus almost to Poupart's ligament. Beneath the skin in this situation can be felt a fibrous cord, and there is no patent internal saphenous. The vein on the right side is patent. On inquiry, the patient says that some three or four years before the onset of his vaso-motor symptoms he suffered from several attacks of acute pain in the left leg, accompanied by great tenderness and some swelling, and lasting from two to three weeks at a time. The last attack affected the inner side of the thigh and occurred within four months of the onset at the ankle. The patient was in good health at the time, had not suffered from typhoid fever, and was certain that there was no sore or wound on the leg. There have been no subsequent attacks, and there is no persistent œdema. No other veins were ever affected.

Case III. Gaz. d. hôp., Paris, 1845, 2. s. VII, p. 86. Jadioux reports a case in a young man aged twenty, with a clear family and personal history. No lues and no suspicion of gout. There was a history of exposure to cold and wet for a short time; but the exposure was not of an extreme nature, was not unusual to the patient, and had never before been associated with disturbances of this or any other sort. On this occasion, after the exposure, the young man was suddenly taken with great pain in the middle of the thigh, abruptly and without any prodromal sensations, and followed by the classical signs of phlegmasia alba dolens. The total duration of the illness was four months, there being two or three distinct phases of acute recrudescence of the venous inflammation, separated by periods of quiescence. The veins affected were apparently the external iliac and crural vessels of the left side. There was no fever or constitutional disturbance at any time, and the patient made a complete recovery.

Case IV. Gaz. d. hôp., Paris, 1864, XXXVII, p. 345. Frémy reports the case of a shoemaker, an old soldier, aged fifty-six. F. H. negative. P. H. Always strong and healthy. Tripper twice, some years before; no lues. Twenty years before was in hospital some weeks with "sciatica"—otherwise had never been sick. There was no suspicion of gout or rheumatism in this patient or his family.

In December, 1861, the patient was taken with sudden lancinating pain in the calf of the left leg. There had been no injury, excessive strain, or local or general infection. The pain became intermittent, was not at any time severe, and disappeared within a week or so. A month later acute pain in the same region was experienced, this time so severe as to incapacitate the patient for work, and swelling and tenderness of the calf were noticed. At the end of two weeks the œdema disappeared, and the pain became slight enough to enable the patient to return to work, though it persisted to some extent. In February, 1862, after a long walk, the patient was again attacked by sudden severe pain in the left leg, from the site of the previous trouble up the inner side of the knee, and along the middle of the thigh towards the groin. On the following day œdema appeared in the foot, soon implicating the whole limb up to the middle of the thigh. The patient was quite unable to work, and one week later was admitted to hospital. Examination revealed an extremely sensitive firm cord occupying the position of the saphenous vein and extending up almost to the level of the saphenous opening. The œdema of the leg was massive, the skin cool. There was no fever and no constitutional disturbance. Mercurial treatment was instituted, and with rest and local applications, the local condition improved. During the patient's stay in the hospital, and after intervals of complete quiescence, he suffered from two recrudescences of the inflammatory condition in the course of the vein previousy affected. Two months after admission the patient left the hospital with the leg in a perfectly normal state. Frémy is disposed to suggest the peculiar sedentary attitude required by the patient's trade as the determining cause of the thrombosis.

Case V. Anfiteatro anat., Madrid, 1880, VIII, pp. 127, 140. E. Delgado-Villadiego reports the case of a man aged fifty-two, corpulent, of sedentary habit, and a gross feeder. He was not luetic, and had a clear family and personal history, with no suggestion of gout or rheumatism. He was

[1] At the present time (April, 1905), this patient has just recovered from a further recurrence of his affection, the first one in nearly four years, implicating one of the small veins on the dorsum of the foot. The onset was typical, constitutional disturbance nil, no local or other cause was present, acute symptoms lasted about ten days, and the occluded, slightly tender vein is distinctly palpable. Dr. T. C. Janeway had recently very kindly put in my way a reference to a case of Dr. Schwyzer's, in which recurrent thrombosis had been associated with a very rapid blood coagulation time, great diminution of chloride output, and calcium retention, proven later to depend on the presence of fluorine in beer drunk by the patient. I was able to investigate these matters in this last attack suffered by my own patient, and found his blood coagulation time in the acute stage to be from 2½ to 3¼ minutes, and his urinary chlorides constantly above 9.5 grammes in the 24 hours. In this connection the low blood coagulation time observed at one examination in Case VII of this series is of suggestive interest.

suddenly taken with pain and swelling in the calf of the left leg, and the first medical man called in wanted to incise what he thought must be a deep abscess. From this time through a period of five months the patient suffered from repeated attacks of clearly recognized thrombo-phlebitis of the femoral veins, both sides being progressively affected, with alternating periods of quiescence and flaring up of the acute symptoms in successively higher stretches of the vessels, until they were both occluded practically up to Poupart's ligament. There was at no time any fever or disturbance of general health. Mercurial treatment was employed, and recovery was satisfactory, with no œdema. The detailed history of the recrudescences is practically that recited in connection with Case I.

CASE VI. Gaz. méd., Paris, 1891, LXII, p. 327. Muselier reports the case of a man aged fifty-eight, not gouty, who had had lues and smallpox many years before. No injury, local or general infection, cachexia or anæmia in connection with his present illness. The patient was taken with sudden intense pain in the left upper arm, with rapidly developing œdema below the site of pain. Thrombosis of the deep brachial vein just below the axilla was made out on examination. Bandaging below the block was resorted to in order to control the massive œdema. At the end of a month recovery was complete, without any succeeding relapses, and no other veins were affected. As in all these cases, constitutional disturbances were marked by their absence. Muselier has no suggestion to make as to etiology. The only plausible cause not absolutely excluded by his report, however, is the very remote possibility of the unrecognized presence of a cervical rib, with consequent pressure. Axillary tumors were excluded. The absence of repeated relapses and new attacks, and the localization in the upper extremity, make this case and the next rather different from the rest.

The following notes concern a case which was admitted to Dr. Osler's service shortly after this paper was first presented to the Johns Hopkins Hospital Medical Society. In the localization of the disease process and in the absence to date of any recurrence the case resembles Muselier's, above. But the clear history, the apparent clinical spontaneity of the lesion and the fact that Dr. Osler and Dr. Thayer both examined the patient, make it seem justifiable to include this case with the preceding one even though the course of events in them does not admit the adjective "recurrent" in the title under which this is written.

CASE VII. A young American, age twenty-two, was admitted to the Johns Hopkins Hospital October 20, 1904 (Hospital No. 48,606), with the diagnosis of thrombosis of the axillary vein. F. H. Negative as regards gout, rheumatism, or other dyscrasias. P. H. Typhoid fever ten years ago; otherwise always healthy. The patient has always been active, is of a slightly neurotic temperament, and is in a business which requires no particularly sedentary or otherwise unusual physical life. No antecedent general or local infection.

P. I. No history of exertion except carrying a suit case while travelling. On October 20, 1904, at 1.30 p. m., the patient remembers shaking hands with a friend, when his arm and hand were quite normal. A little later, on again shaking hands, he felt a slight twinge of pain in the right elbow and a sensation of coldness in the hand. Half an hour later the hand was distinctly swollen and very numb. The patient immediately consulted a physician and while with him the circumference of the right arm increased one inch in half an hour. Massage was tried without benefit; as the œdema was rapidly increasing the patient came to Baltimore and saw Dr. Thayer. He was admitted to the hospital at 10 p. m. of the same evening.

At 8 p. m. Dr. Thayer made the following note: "Healthy-looking man; right arm, forearm, and hand greatly swollen and of deep-blue cyanotic color and quite cold. The peripheral veins from the hand up are prominent and exceedingly tense. In the outer axilla the vein stands out suddenly and sharply as a hard knuckle—clearly the beginning of the thrombus. The swelling extends up over the deltoid region and is perhaps more marked in the upper arm. The measurements, 20 cm. below tip of acromion are, on the right, 33.4 cm., on the left, 26.5 cm. The right radial is palpable."

The next day Dr. Osler made this note: "Arm not so livid as last night. Veins on back of hand not so prominent. Hand is warm. Diffuse redness up to middle of arm. Radial well felt. There is a line of demarkation of redness above insertion of deltoid. No soreness of clavicle."

The temperature ranged from 98° to 99.6° for the first six days and was normal continuously after October 26. The urine was negative. On October 21 the leucocytes were 11,600. On October 25, 12,700.

On October 25 I saw the patient in the ward, when his arm was in the condition above described. Pain, which had been considerable for the first few days, was becoming less, though the arm was very tender to touch and even slight passive motion caused distress. A most interesting feature that is not noted in the history was that the patient had, for so young a man, a very marked degree of sclerosis of the superficial veins of both upper and lower extremities—a fact that cannot but be of really considerable significance. On October 25 the coagulation time of the patient's blood was between one and a half and two minutes.

On November 17 the patient's improvement having been steady if gradual, and the arm apparently normal, the patient was discharged. No note was made at this time of the condition of the vein at the point of blocking. There had been at no time any constitutional symptoms other than those of a neurotic nature.[2]

There have been in the hospital recently two very interesting cases of femoral phlebitis whose records I have had the privilege of examining. One of these, a man who was in

[2] Dr. H. W. Cook, who has recently (April, 1905) seen this patient, informs me that the fibrous cord of the obliterated vein is easily felt and identified in the patient's axilla.

Ward F in September, 1904, died suddenly from embolism of the pulmonary artery. In neither of these house cases was the cause of the thrombotic process definitely determined; but as both patients had some pus in the urine, and as their phlebitis was attended by some fever and other general constitutional symptoms, it has been thought best not to attempt to include them in this series of cases.

These seven cases constitute the whole of the material that I have to report. There are hosts of articles scattered through the literature professing to deal with instances of spontaneous phlebitis, but on going through these papers it is found in nearly every instance that the authors are reporting cases of phlebitis in association with anæmia, typhoid fever, or other infections or cachexiæ, or cases in which these or some of the other recognized factors in the production of thrombotic processes cannot be excluded. I have included no cases in which the epithet "spontaneous" has not seemed beyond criticism just, in the present state of our knowedge. The only other instances of which any record has been available are those reported in the thesis of Daguillon.[3] He details accounts of five original cases, resembling in all essential particulars those reported here, except that the author feels constrained, or enabled, to label all the patients "non-gouty arthritics," and refers these and seven other cases collected from the literature, to the influence of the lithæmic diathesis. It is interesting that of the twelve cases reviewed by the French author, three died of embolism, and there were altogether six patients afflicted with embolic sequelæ of greater or less severity. Some of Daguillon's conclusions are of interest. He says:

"There is a primitive form of phlebitis, *i. e.*, one without any immediate determining cause."

"Primitive phlebitis is an indication of a general diathetic influence, shown in an arthritic constitution, with or without actual gout."

"It has a special clinical picture—that of limited, localized, superficial phlebitis, affecting the lower limbs, causing slight local and no general reaction. It is of slow evolution, and shows a progressively ascending march by successive attacks and relapses."

"The prognosis is serious, owing to the facility with which embolism occurs."

Daguillon believes that the process is mainly a parietal thrombosis, and that complete and final fibrous obliteration of the vein occurs as rarely as does suppuration, which is never. In the cases which I have been able to examine, there has been no doubt possible as to the permanent obliteration of the vein after the subsidence of the acute process, and this seems to have occurred just as certainly in the cases collected here from other sources.

It is as well to admit without reserve that the picture here presented is practically identical with that described by Paget[4] for gouty phlebitis, and that I can find no other variety of phlebitis from any cause running such a peculiar and characteristic course. But that does not seem sufficient cause for following Daguillon, and subscribing to Tuckwell's dictum, that all so-called spontaneous phlebitis is in reality the phlebitis of gout. It may be considered suggestive that one of the present series was a sufferer from Raynaud's disease, which Haig at least would definitely associate with the state of uricacidæmia. But that particular instance is one of the least satisfactory here reported, and could be dropped from consideration, and still leave a body of cases in which the ascription of the lithæmic, or of the even more generously inclusive "neuro-arthritic," diathesis, would require a facile imagination. It is true that Hirtz and Hannequin,[5] in a suggestive paper on venous heredity, hold that among arthritic families the diathesis may manifest itself solely by a tendency to varices and to phlebitides from slight causes, with great liability to relapse of the latter. They wish to connect the tendency with a general condition of weakness of the connective tissues in these families, and report cases of phlebitis from different causes occurring with unusual frequency in members of the same family.

A family and personal history of great interest in this connection has been referred to me by the kindness of Dr. Wilder Tileston of Boston. The patient, a man of thirty-five years, has since 1887 passed through eight attacks of thrombophlebitis in the lower extremities, almost without doubt of the same type as the series reported. The case is not included with the indubitably "idiopathic" group at this time, because it is vaguely possible that some at least of these eight thromboses may have been associated with an anæmia. Of sixteen adult individuals among this gentleman's ancestors and collateral relatives, eight have shown a marked susceptibility to venous disease, in the manifestation of varices and hæmorrhoids or in extreme liability to thrombosis in the puerperium or following the acute infections. In other respects, the family history seems beyond the grasping criticism of the uricacidists.

However valid Hirtz and Hannequin's assumption may be for the cases they report, and without accusing the more fervid of the supporters of the lithæmic diathesis of attempting to make it cover too great a variety of physiological sins, it certainly seems unlikely that the present cases can be brought under the arthritic ban. Excepting the case with symmetrical gangrene, not one of the patients showed any manifestation either of gout or of the large number of ills that have been referred to uric acid; in all the cases, the family histories were quite clear of anything referable to this taint. It does not appear to be justifiable to qualify a phlebitis as gouty, simply and purely because it is apparently spontaneous, nor altogether because of its similarity in course to other inflammatory conditions of supposedly gouty origin.

Admitting then, for the moment, that we are ignorant of the pathology and causation of the cases here considered, the

[3] Thèse de Paris, 1894.

[4] St. Bart. Hosp. Reports, 1866, II, p. 82.

[5] Bull. méd. Paris, 1901 XV, p. 389.

following etiological suggestions may not be out of place. We are familiar with the predilection of thrombotic processes within the arteries for such portions of the vessel wall as are affected by arterio-sclerosis. The acute and inflammatory affections of the endocardium are specially prone to attack valves already damaged, by preference over those with unaltered endothelial coverings. We also know that phlebosclerosis is a condition quite analogous anatomically to arterio-capillary fibrosis, that it is frequently associated with the latter condition, may occur very early in life, and has hitherto attracted rather a curious interest, as having no particular significance. May it not be that the cases of venous thrombosis with which we are dealing depend for their immediate and localizing cause on such sclerotic changes in the walls of the veins? If a cachexia may determine the production of a thrombus within an artery, it seems very easy to believe that with the much slower current of the blood within the veins, an extreme or even beginning phlebo-sclerotic change might determine the deposition of a fibrin coagulum from the blood stream. Sclerotic alterations of the vein walls are often observed to progress by fits and starts, at times with great rapidity, and then to remain in a stationary condition for many years. It is suggested that such a rapidly progressive stage of the fibrosis, if associated with a small, even at first a purely parietal thrombus, might produce just such a series of phenomena as are shown by the present group of cases. The often insignificant—and probably often unrecognized—symptoms of the first onset, the peculiar progression of the affection through the continuity of the same vessel, successively attacking higher and higher stretches of the damaged vein, the almost constant story of good general health during and between the attacks—all these considerations suggest that if a constitutional fault, a diathesis, is at the bottom of these apparently idiopathic occurrences, that diathesis or fault is far more likely to be one concerned with the wall than with the contents of the vessel. It is an anatomical, rather than a chemical, depravity, of the constitution that is the affliction of these patients. It is realized that all this is very theoretical pathology—it is put forth very tentatively, subject to critical correction, and with hope that actual laboratory studies of the true pathological condition will serve either to substantiate or to correct the views so roughly sketched. It is noteworthy that all of the cases which I have been able to examine showed beginning sclerotic changes in the superficial veins of the extremities, in association with some degree of thickening of the arteries, though in only one instance (Case VII) was the change at all extraordinary, being in the others less than is seen every day in a multitude of persons who so far as we know have never suffered from thrombosis. The absence of fever and the fact that suppuration of the thrombus has never been observed in these idiopathic cases would support the view that they are not caused by obscure infections.

In conclusion, it may be noted that the prognosis of idiopathic recurrent thrombo-phlebitis is, as given by Daguillon, rather unnecessarily grave. Twenty-five per cent mortality seems extraordinarily high, and may probably be ascribed in his series to the fact that from their very nature, and the usual relative mildness of their symptoms, the large majority of these cases that occur will fail to find their way into medical literature. Some at least of the patients may walk about with an actively progressing thrombosis. That this may, with those ignorant of their risk, increase the danger of embolism over that suffered by the recumbent typhoid patient with phlegmasia, is unquestionable. It is also beyond doubt that a thrombus will often stand a great deal of manipulation. Still, none of us would care to allow a subject of this affection to roam about with no restraint but that imposed by pain, considering the recorded score of fatalities as it stands at present. And yet the alternative, that a busy man should be kept idle or recumbent for a long period, that may extend over the greater part of six months, by an affection in itself almost insignificant, seems ridiculous. An attempt to carry out such a measure with the average American would undoubtedly end in failure, and might result in sending the patient into other and less careful hands. When an obliteration of the lower part of the saphenous vein occurs in an otherwise healthy man, and is followed after recovery and a period of quiescence, by a second apparently spontaneous phlebitis in a higher part of the vessel, it would appear to be advisable to cut down over the saphenous opening under cocaine, and to ligate the vein at its termination. Such a procedure would at once obviate any further danger of embolism, and would necessitate only a short and definite period of confinement. When the phlebitis starts out in the very characteristic fashion above described, the chances are strong against it stopping short of the upper part of the thigh; the vein is doomed in its whole ength, and in any case its dangerous contents could be more comfortably supported with a firmly tied knot of good silk between it and the lungs.

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A REPORT OF SOME OBSERVATIONS ON HEART-BLOCK IN MAMMALS.[1]

By Joseph Erlanger, M. D.,
Associate in Physiology, The Johns Hopkins University.

Through the courtesy of Dr. Osler the author has had the opportunity of making observations on a case of Stokes-Adams disease in which the disturbances in the circulatory system obviously owed their origin to the condition now generally termed heart-block. The studies made of this case indicate that when the block is complete the auricles respond normally to influences exerted upon the heart through its extrinsic nerves; but the ventricular rate seems to be influenced neither by changes in posture, nor by atropin, nor by moderate muscular exercise. However, the ventricular rate may be increased by more severe muscular exercise. On the other hand it could be shown that when the block is partial not alone the auricles but also the ventricles, the latter within certain limits, respond normally to extrinsic influences. The characteristic attacks of unconsciousness are always associated with a very marked slowing of the rate of the ventricle; the intervals between the beats may be twelve seconds. The slowing of the ventricular rate always precedes the cerebral symptoms by an appreciable interval.

These observations led to an attempt to produce and to study heart-block in mammals by methods that do not involve destruction of all the tissue in a cross-section of the heart.

After having made some preliminary and more or less successful attempts to produce heart-block in the dog, a simple and satisfactory method was devised of clamping the limited region in which lies the only muscular connection between the auricles and the ventricles, the auriculo-ventricular bundle of His. The method is not particularly difficult, and since it has been perfected the clamp has been successfully applied in every attempt.

When the clamp has been put in the right place the heart will continue to beat with undisturbed rhythm. But when the arms of the clamp are cautiously screwed together, the normal sequence of the auricular and ventricular beats will more or less abruptly give way to a partial block in which the beats of the auricles are to the beats of the ventricles as 2 : 1. With further clamping a 3 to 1 rhythm may be established and this, as a rule, passes into complete block in which the beats of the ventricle are totally independent of those of the auricle. The reverse order of changes is obtained when the clamp is unscrewed. As a rule the changes of rhythm occur at once, that is, without a preliminary stoppage of the ventricle.

In two experiments upon tightening the clamp the normal sequence gave way to complete block without passing through the usual intermediate stages. In these instances at the moment the complete block was established the ventricular rate was markedly slowed and the blood-pressure fell to a very low level. Thus in one of the instances the interval between two ventricular contractions was twenty-one seconds. The ventricular rate and the blood-pressure then gradually increased until values usual for heart-block were reached. The exact cause of this phenomenon has not yet been determined.

With each change in rhythm the blood-pressure is materially affected, falling when the ventricular rate is decreased and rising when the ventricular rate is increased. But even in complete block a fair pressure may be maintained.

When the block is partial both the auricle and ventricle may be inhibited by stimulation of the vagus nerve at least as easily as under normal conditions. But when the block is complete no diminution, or but very slight diminution of the rate of the ventricle results from stimulation of the vagus. The auricles react normally to vagus stimulation. Section of both vagi has little or no influence upon the rate of the ventricle when the block is complete.

Stimulation of the accelerator nerve as a rule increases the rate of the ventricle in complete block. The increase may be as great proportionally as that obtained under normal conditions. The reaction of the auricles to stimulation of the accelerator is not influenced by the block.

The rate of the ventricle in complete block is not as a rule materially affected by variations in the blood-pressure produced, for example, by compression of the abdominal or thoracic aorta or by extreme hæmorrhage.

The plugging of one coronary artery, either the right or the left, by Porter's method, has not obviously altered the rate of the ventricle in complete block.

In every case of failure to obtain block in the preliminary experiments it was found at autopsy that the ligature or clamp had not been placed so as to grasp the region of the auriculo-ventricular bundle.

The analogies between the phenomena of heart-block in the dog and the signs and symptoms of Stokes-Adams disease are obvious, and we may therefore be justified in predicting that the location of the lesion will be found to be the same in both conditions.

[1] Abstract of paper read before the Johns Hopkins Medical Society, March 20, 1905.

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THE FORCE OF CONTRACTION OF THE GALL-BLADDER AND THE COURSE OF ITS MOTOR AND INHIBITORY NERVE FIBERS.

By J. A. Freese.

(From the Physiological Laboratory of the Johns Hopkins University.)

In response to an inquiry from Professor Halsted regarding the force of contraction of the gall-bladder it was found that no data could be obtained from the literature, bearing upon this point. The series of experiments described below was therefore undertaken in the physiological laboratory under the direction of Professor Howell for the purpose of determining the force of contraction of this organ. The work was afterwards extended to take in a study of the path of its nerve fibers, since evidence was soon obtained that the musculature of the bladder is supplied with inhibitory (or dilator) nerve fibers as well as with motor (or constrictor) fibers.

Method of Recording the Movements of the Gall-Bladder.

All of the experiments were made upon dogs. The animals were given one grain of morphia hypodermically an hour before the operation began. Throughout the experiment complete anæsthesia was maintained by administering ether through the trachea from an ether bottle. A metal canula was introduced into the gall-bladder and was then connected by means of lead tubing with a suitable water manometer. This manometer was provided with a float, bearing a pen for recording the changes in pressure. The canula and tubing throughout was filled with Ringer's solution.

The canula, about 20 cm. long, was made of brass tubing with an outside diameter of 3.25 mm. and a bore of 2.7 mm. in diameter. The end of the canula inserted into the bladder was slightly bent and was provided with three openings. To insert the canula the duodenum was cut open opposite the mesenteric attachment, and the papilla showing the opening of the bile duct was found. Through this opening the canula was introduced into the duct and pushed carefully along until its bent end lay well in the interior of the bladder. The canula was fastened by a ligature applied to the bile duct just outside the duodenum. Some difficulty was experienced at first in obtaining a perfectly accurate recording float, but the device shown in Fig. 1 was finally adopted, and has proved so satisfactory that it merits a special description. This float is made of a gelatine capsule, as follows: The top of a No. 3 capsule is removed and a hole about 0.7 mm. in diameter is bored through its center. The cap piece of a No. 4 capsule is then taken and prepared with a similar hole in its center. It is trimmed as much as possible, until only the cap-like end with its central hole is left. This latter piece is shoved into the bottom piece of the No. 3 capsule; the cap-piece of which with its central opening is then put in place. The stem of the float consists of a slender glass rod prepared from tubing by drawing it out in a flame. This stem is shoved through the hole in the top of the capsule and then down through the hole in the cap-piece previously inserted into the bottom of the capsule. The stem is thus held firmly at two points. The upper end of this stem, after passing through the cap of the manometer is bent at right angles and drawn out to a writing point, which is kept against the smoked surface of the drum by a pendent weight. As the gelatine is soluble in water it is necessary to keep a layer of olive oil on the surface of the salt solution in the manometer. In practice a layer of oil of about 60 mms. or more, was used. This required about 2.5 to 3 cc. of oil. The lighter specific gravity of the oil was compensated nearly exactly by the weight of the float and stem so that the results obtained can be expressed in terms of millimeters of salt solution. In all the experiments made upon stimulation of the spinal nerves it was necessary to curarize the animal in order to avoid the mechanical effects of contractions of the trunk and abdominal muscles. A one per cent solution of curare was used, made up in normal saline. This solution was injected into the jugular vein until stimulation of motor nerves failed to give a muscular response. Artificial respiration was then maintained with warm moist air.

The Force of the Muscular Contraction of the Bladder.

As stated above no record could be found in the literature of experiments made to determine directly the force of contraction of the muscles of the gall-bladder.

Heidenhain, Friedlander, and Barisch have measured the secretion pressure of bile.[1]

Heidenhain determined the pressure in connection with that of the superior mesenteric vein as proof that bile is not formed by simple filtration from the blood. His results show that the secretion pressure may vary from 110 to 220 mms. of a solution of sodium carbonate. The experiments of Friedlander and Barisch were made upon guinea pigs. A canula was inserted directly into the bladder and the bile duct was tied off at the intestine. The maximum pressure found varied from 184 to 212 mms. water.

In my own experiments secretion pressure was of course excluded. To obtain if possible a maximal contraction of the gall-bladder the splanchnic nerve was stimulated by strong

[1] Heidenhain in Hermann's Handbuch der Physiologie, Vol. 5, part 1, p. 269 and Friedlander and Barisch, Reichert and Du Bois Reymond, Archiv für Anatomie und Physiologie, etc., 1860, p. 646.

induction shocks, or the electrodes in some cases were applied directly to the neck of the bladder, or finally the spinal nerves were stimulated. The bladder in all cases was put under a certain pressure to start with, and in estimating the work done by the contraction this pressure must be added to the actual increase caused by the contraction. Some of the experiments were made with curare and some without. When curare is not used care must be taken not to allow an escape of current to the muscles of the diaphragm or to sensory surfaces that might reflexly cause a contraction of the diaphragm. For a typical gall-bladder contraction see Fig. 2.

While numerous experiments were made, results that bear upon the present question were obtained only in six cases, as follows:

Animal	Point of applying stimulus	Bladder under a pressure of	Rise	Total Pressure
	Without Curare			
Dog 16	Electrodes on bladder	305. mm.	7. mm.	312. mm.
Dog 17	" "	305. mm.	8. mm.	313. mm.
	With Curare			
Dog 18	Peripheral end of splanchnic	190. mm.	26. mm.	216. mm.
Dog 25	Combined result from stim. 8 and 9 dorsal	197. mm.	21. mm.	218. mm.
Dog 26	Stim. L. splanchnic	200. mm.	14.5 mm.	214.5 mm.
Dog 28	" "	217. mm.	4. mm.	221. mm.

Since the results in the last four experiments were obtained under conditions in which the possibility of error from direct or reflex stimulation of the skeletal muscles was entirely excluded they give perhaps the most reliable data concerning the force of contraction of the bladder.

It appears from these results that the bladder is capable of contracting against a resistance such as is offered by a column of Ringers solution 214.5 to 313 mm. high. Moreover the sudden maximum increase of pressure from direct stimulation of the peripheral end of the splanchnic apparently falls below 30 mm. when the pressure against which the bladder is working is about 200 mm. It seems evident from these figures that the musculature of the bladder is comparatively weak and that its contractions are not at all comparable in force to those of the urinary bladder, which, according to Mosso,[2] may contract in the dog with a force sufficient to support a column of water two meters high. Indeed the maximum force of contraction of the bladder does not much exceed the maximum secretion pressure as determined by Heidenhain.

The Motor and Inhibitory Nerve Fibers to the Gall-Bladder.

It has been shown by Heidenhain,[3] and especially by Doyon[4] that the gall-bladder and the bile ducts receive motor fibers by way of the splanchnic nerves. On stimulating the peripheral end of the splanchnic they got a contraction of the bladder. Doyon found also that stimulation of the central end of the splanchnic causes a reflex dilatation or inhibition of the bladder, but he was not able to obtain this inhibition by direct stimulation, that is, he got no evidence of the existence of peripheral inhibitory fibers. In some of my earlier experiments the stimulating electrodes were applied directly to the neck of the bladder where it passes into the cystic duct. It was found in some cases that when the electrodes were applied to the ventral side contraction of the bladder resulted, whereas, when placed upon the dorsal or dorso-lateral side a dilatation ensued (see Fig. 4). This result indicated the existence of inhibitory as well as motor fibers and an effort was made to trace out the origin of these two sets of fibers from the spinal cord with the hope that they might emerge by different roots. In later experiments the existence of inhibitory fibers in the splanchnic nerve was demonstrated successfully (see Fig. 5). Usually when the splanchnic nerve is cut and the peripheral end is stimulated by strong tetanizing currents a constriction of the bladder results; in some cases, however, the constriction is followed by a marked dilatation, and in other cases a marked dilatation only is obtained.

This latter result was obtained with dogs under morphia and a strong dose of curare. It seemed evident from these results that the splanchnic nerve is capable of causing either a constriction or a dilatation of the gall-bladder, and therefore probably contains both motor and inhibitory fibers for this organ. To ascertain the point of emergence of these autonomic fibers from the spinal cord numerous experiments were made. The procedure was as follows: The spinal cord was exposed with great care, and the hæmorrhage that occurred from the bones was controlled as the operation proceeded, so that the total loss of blood was quite small. The exposure was made for the region of the lumbar and lower thoracic nerves in some cases and in others for the lower and middle thoracic nerves. The spinal nerves on one or both sides were prepared and a ligature placed around each. No attempt was made to separate the anterior and posterior roots since in some of the animals at least it was not found possible. After the nerves were prepared the abdomen was opened and the canula was inserted into the bile duct and connected with the manometer as described above. Curare was then administered through the jugular vein until stimulation of motor nerves gave no response. Artificial respiration was maintained with warm moist air. After the curare effect was fully manifest the spinal nerves were stimulated as follows: Each nerve was ligated close to the cord and then cut between the ligature and the cord. The effect of this mechanical stimulation was noted and an interval of several minutes was allowed between each ligation. Afterwards the spinal nerves were stimulated in order, with an interval of four or five minutes between each stimulation. The electrodes used were carefully shielded with paraffine to prevent escape of current to the cord and induction currents of various strengths and rate were used for stimulation. It was not found, however, that rate of stimulation made any difference in the result, except that below a certain rate a stimulus otherwise effective

[2] Mosso and Pellacani, Archivs italiennes de biologie, I, 307, 1882.
[3] Studien des physiologischen Institut zu Breslau, 1860.
[4] Archives de physiologie, normale et pathologique, 1894, p. 19.

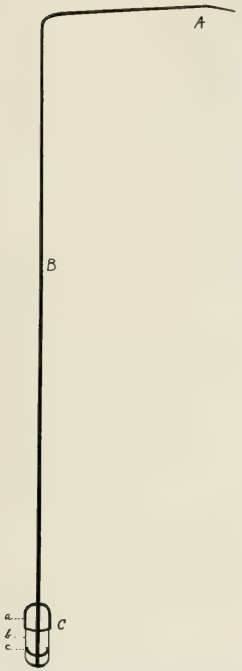


FIG. 1.—To show the float devised for this work, *A* is the writing point, *B* is the perpendicular stem, and *C* is the gelatine capsule. The top of the No. 3 capsule is designated by *a*, and its bottom by *b*. The inserted top of the No. 4 capsule is seen at *c*.

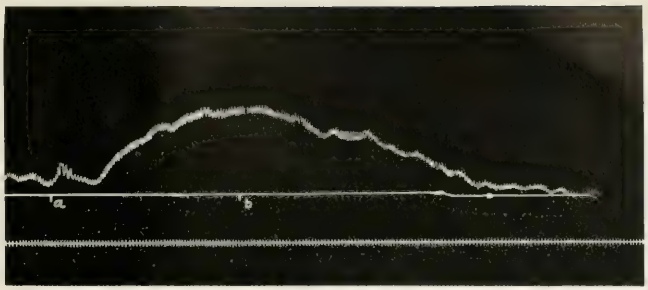


FIG. 2.—To show a typical gall bladder curve, resulting from stimulation of the peripheral end of the left splanchnic. Medium current on at *a* and off at *b*. Dog under curare. Time record indicates intervals of three seconds.

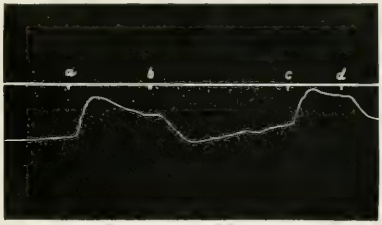


FIG. 3.—To show contraction upon applying the electrodes directly to the neck of the gall bladder. Stimulus on at *a*, off at *b*. Repeated for check (see *c* and *d*). This contraction was obtained in a curarized dog ten minutes after the animal had been bled to death by cutting the carotid.



FIG. 4.—To show dilatation upon applying the electrodes direct to the neck of the gall bladder. Dog under morphia and ether.

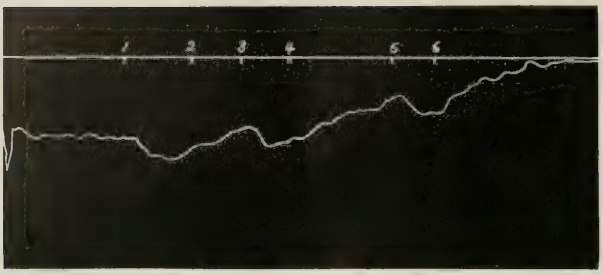


FIG. 5.—To show dilatation upon stimulating the peripheral end of the splanchnic. First stimulation (1 to 2), second stimulation (3 to 4), third stimulation (5 to 6). It will be noticed that there is also a gradual increase in bladder tone resulting from the repeated stimulation. Dog under curare.

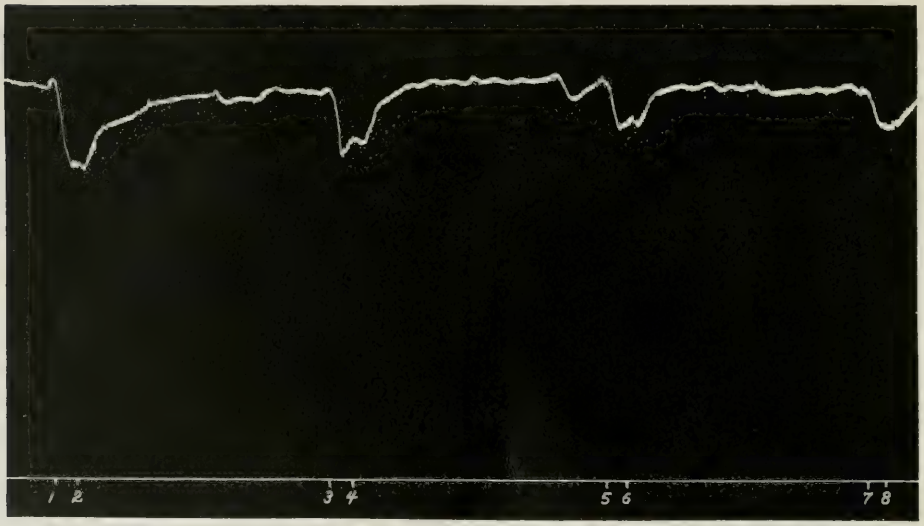


FIG. 6.—To show the dilatation upon stimulation of the spinal nerve roots. Stimulation of the eighth spinal nerve root (1 to 2). Stimulation of the ninth spinal nerve root (3 to 4). Stimulation of the tenth spinal nerve root (5 to 6). Stimulation of the eleventh spinal nerve root (7 to 8). Dog under curare.

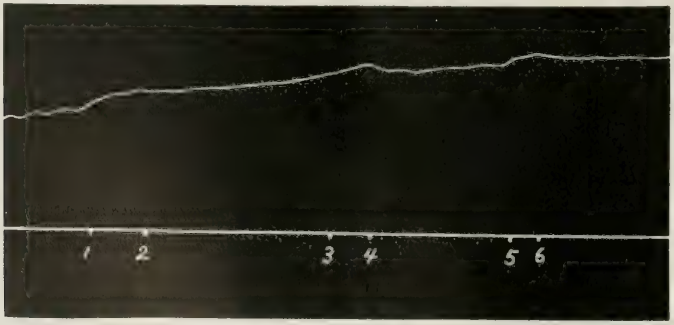


FIG. 7.—To show the contraction on stimulation of the spinal nerve roots. Stimulation of the twelfth spinal nerve root (1 to 2). Stimulation of the eleventh spinal nerve root (3 to 4). Stimulation of the tenth spinal nerve root (5 to 6). Throughout there is a constant increase in tone of the gall bladder due to repeated stimulation. Dog under curare.

became ineffective. As a result of this work it was found that the motor and inhibitory fibers leave the spinal cord in practically the same region, namely, from the sixth or eighth thoracic to the thirteenth thoracic spinal nerve. In some animals chiefly inhibitory effects were obtained, especially as the result of the mechanical stimulation on tying the roots. In others only the constrictor effects were shown. The results as regards the lower limit of emergence of these fibers were clear and constant. In no experiment were any effects upon the gall-bladder obtained below the thirteenth thoracic or first lumbar nerve. The upper limit was not defined so satisfactorily. In one case dilatation was obtained as high as the sixth dorsal and constriction as high as the seventh dorsal. The main outflow of the constrictor fibers occurs in the tenth, eleventh, and twelfth dorsal spinal nerves (see Fig. 7). The dilator fibers are most in evidence from the eighth to the twelfth dorsal nerves (see Fig. 6).

In these experiments the possible effect of contraction of the skeletal muscles upon the gall-bladder was eliminated, it is believed entirely, by the use of curare. It might be objected, however, that the variations in pressure in the bladder which were taken as proofs of constriction or dilatation as the case may be, might have arisen as the result of vaso-motor action upon the bladder or upon the liver. In connection with this possible objection it is interesting to state that upon several occasions both constriction and dilatation of the bladder were obtained upon stimulation of the splanchnic nerves after the animal had been bled to death (see Fig. 3). This fact would seem to show that the variations of pressure in the gall-bladder observed during these experiments were actually due to the contraction or relaxation of the musculature of the bladder itself.

Conclusions.

1. When stimulated through its motor nerves the bladder is capable of contracting against a pressure of at least 220 mms. of Ringer's solution, specific gravity 1.004. The maximum force of contraction exerted by the gall-bladder does not exceed materially the maximum secretion pressure of the bile.

2. The musculature of the gall-bladder is provided with motor (constrictor) and inhibitory (dilator) nerve fibers. These fibers are found in the splanchnic nerves.

3. Both the motor and the inhibitory fibers arise from the spinal cord in the roots of the sixth to the thirteenth dorsal nerves. The maximum outflow for the constrictor fibers is in the tenth, eleventh, and twelfth dorsal nerves. The dilator fibers appear slightly higher up and are most in evidence from the eighth to the twelfth dorsal nerve inclusive.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

April 3, 1905.

Sarcomatous Myoma.[1] Dr. Cullen.

Dr. Cullen showed a specimen of this condition, removed from a woman of forty-two. Two years ago she had presented the usual features of a myomatous uterus which, with the subperitoneal nodule above it, was removed by the usual operation. The tumor was thought to be myomatous. In February, 1905, she was seized with sudden pain in the lower abdomen and was operated upon again. The abdomen was found filled with blood, and sarcomatous nodules were discovered springing from the cervix. Complete removal was impossible. Examination of the tumor removed at the first operation and thought to be a simple myoma showed sarcomatous degeneration.

Fibroma of Abdominal Wall.[1] Dr. Cullen.

This had been removed from a woman thirty years of age. Three years previous she had noticed a mass under the ribs which had grown slowly at first and later more rapidly. There had been some loss in weight. At operation a fibroma was found springing from the muscle sheath.

Primary Carcinoma of the Tubes.[1] Dr. Cullen.

The growth in this case had started from the Fallopian tubes, had involved the ovaries and studded the omentum. Pain on defecation had been a prominent symptom. A complete hysterectomy was done and six inches of bowel removed, the sphincter ani being preserved. The patient is still alive and feels well.

[1] These cases will be reported in full later.

Accessory Omentum. Dr. Cullen.

A railway conductor, following a struggle with a drunken passenger, was seized with abdominal pain, showed a temperature of 101.5° and a leucocytosis of 17,000. There was no abdominal rigidity but an exploration was advised, and at operation a greyish mottled mass was found which proved to be a twisted accessory omentum arising from the union of the ascending and transverse colons.

Dr. Kelly, in commenting on Dr. Cullen's first case, said that the interesting question was now raised as to which myomata could be regarded as simple and treated as non-malignant, and in which ones the prognosis was bad. At any rate in these cases the uterus should always be laid open and examined carefully before the abdomen is closed. It is important also to determine how far these growths extend, for if they involve the mucosa the wisdom of supra-vaginal amputation—otherwise the operation of choice—would be doubtful.

The Electrical Theory of Matter. Prof. H. C. Jones.

Prof. Jones of the Johns Hopkins University gave a somewhat popular exposition of the recent work on radio-activity.

The great problem of physics had always been, he said, to know whether there were several different elements or whether at bottom all were really one. Hydrogen, in early history and later other elements, had been thought to be the fundamental substance. The study of radio-activity really started with the work of Thomson who, working over the question as to whether or not the atom might be the ultimate unit, elaborated the corpuscular theory which defined the corpuscles as little pieces of matter carrying unit electrical charges and as really the ultimate units of matter. The mathematicians then showed that to account for the properties of the corpuscle no matter was necessarily assumable. Unit electrical charges moving at a high velocity through an elastic medium gave all the properties of mass and inertia which we ascribe to matter. This theory is now generally accepted. Following the work of Thomson came the discovery of X-rays by Röntgen. Then Becquerel found a remarkable radiation produced by uranium, and Schmidt, by thorium. This led to a careful study of pitch-blende by the Curies and the discovery of radium.

The Properties of Radium.—The element owes its interest to the fact that it does things no other form of matter does and to a degree never dreamed of. Its first remarkable property is its unique ability to transform itself into another element—helium. Its second phenomenal attribute is its ability—also absolutely unique—of giving out tremendous amounts of heat. These properties of the salt inhere not in the radium itself but in an "emanation" which may be distilled over from the radium bromide and which is constantly being "re-created" in exhaustless amounts. The "emanation" is also the source of the remarkable α, β, and γ rays; and it seems probable that a large part of the sun's heat may be due to the presence in it of radium in quantity.

Experiments on Amphibian Embryos. Dr. Lewis.

These experiments, reported by Dr. Lewis, were undertaken by him to throw, if possible, some light on the problems of preformation and epigenesis. The development of the lens and cornea were studied. The animals were operated on at the time of closure of the medullary groove and the object of the first series of experiments was to see whether a lens would arise from the ectoderm without the presence of the eye. A subcutaneous excision of the eye was done and the skin returned to its place. Serial sections of the animal were then examined at a later stage and no lens was found unless the eye had regenerated. In another series of animals the eye was transplanted, and in many of these cases a lens developed from the ectoderm over the misplaced eye. Even when an eye from one species was transplanted under the skin of another a lens, remarkably enough, was often found to develop. All the findings of the experiments spoke for epigenesis as against preformation.

April 17, 1905.

Comparative Surgery. Dr. Cushing.

The meeting was devoted to comparative surgery, a report being made of the work done in the course in operative surgery on animals by the third-year class of the Johns Hopkins Medical School. Dr. Cushing, by way of introduction, emphasized the importance of building up a veterinary hospital in connection with surgical teaching—not only for the teaching purposes proper but also by way of disarming the criticism, perhaps a just one, which was made against the reckless use of material involved in allowing students to operate on healthy animals. Operative surgery was usually taught by work on the cadaver; it was therefore confined to operations on the extremity and ligation of arteries. But the absolutely essential instinct for surgical cleanliness, the ability to handle living tissues, skill in controlling hæmorrhage—these things could not be learned from a cadaver. Nor was it possible to teach or to learn visceral surgery in this way.

When the course in animal surgery at the medical school was started, operations were done for hypothetical lesions. The material was not then necessarily wasted but could often be used in one of the laboratories; a gastrostomized dog, for instance, furnished the physiologists with gastric juice for study, and so forth. Nevertheless, this method involved needless operation; and criticism of this feature only began to be disarmed when animals were brought in with lesions which needed treatment. In the future, then, the plan is to build up a veterinary hospital so that animals may receive necessary surgical attention and students may receive useful surgical instruction at the same time.

Hæmorrhagic Cysts of the Thyroid.—Mr. Faris reported two cases of this condition occurring in dogs. The first was in an Irish setter. It had caused interference with respiration and cure was effected by its removal. The second occurred in a hound, was associated with bad temper, muscular twitching, loss of hair, increase in weight, and dryness of skin. No exophthalmus was present. The cyst was removed but without much improvement in the dog's condition. Both tumors proved to be thick-walled cysts containing dark-red grumous material made up of shadows of red-blood cells and cholesterin. The pathology of the thyroid in dogs was said to be similar to that in man. Hæmorrhagic cysts, while rare, were occasionally reported. Their etiology was still undetermined. Trauma probably plays a part, and changes in the vessel walls with rupture probably do the rest.

Utero-Vaginal Prolapse.—Mr. Thacher reported two cases. The first was an acute one complicating labor in a bitch. The vagina and cervix were prolapsed, the bladder was out of the pelvis, there was inability to urinate, and the animal was in bad condition. A uterus containing nine pups was removed and the prolapse reduced. Death occurred in fifteen hours, hydronephrosis and localized peritonitis being present. In the second case an irreducible mass protruded from the vulva and two operations were required to cure the condition.

Obstetrical complications were said to be common in animals and death often occurred without delivery. Acute prolapse was most frequent in the herbiverous animals and the immediate cause was often a very full uterus.

Inguinal Hernia in the Dog.—These cases were reported by

Mr. Beall. The first patient showed an irreducible right inguinal hernia with cystocele and the radical hernia operation was done. Death occurred on the second day; the dog showing ulcers of the stomach and an atrophied right kidney. The second patient had a bilateral inguinal hernia. The two sides were operated on at intervals and complete cure resulted. In the third dog the hernia contained the omentum and the round ligament. Hernia in the dog is a very common condition, the commonest variety being the mid-ventral. The inguinal form occurs much more often in the female than in the male, due probably to the occurrence of pregnancy and to the fact that normally a bitch has practically a patent canal of Nuck. In the male, too, the tunica vaginalis retains its connection with the peritoneum so that the anatomical facts alone do not explain the occurrence of inguinal hernia, which is relatively rare in male dogs.

Canine Tumors.—This series was reported by Mr. Ortschild. The first was an adeno-carcinoma of the breast with glandular metastasis. The complete operation was done. Death occurred from cancrum oris. Mixed teratomata over the breast and thorax were found in the second case. These on section showed cartilage, adeno-carcinoma, carcinoma simplex, and bone. In another dog a cyst adenoma of the breast was found and removed. This patient died from a phagadænic ulcer of the mouth. In a fourth case a mixed tumor of the breast, which had succeeded to a "milk-breast" following a bite, was found and removed. Cure resulted. An intracystic papilloma of the breast with metastases, a fibro-lipoma of the vaginal wall, and a hygroma of the right shoulder were also reported. The last tumor of the series was a pedunculated growth arising from the lower abdomen and just swinging clear of the ground when the dog walked. It was removed and proved on section to be an adenoma. Tumors—particularly carcinomata of the skin and mammæ—are common in dogs. Fibromata, enchondromata, and sarcomata of the breast are also seen.

Dr. Bloodgood showed the specimen of a melano-sarcoma of the liver occurring in a horse.

NOTES ON NEW BOOKS.

The Follies of Science at the Court of Rudolph II, 1576-1612. By Henry Carrington Bolton. (*Milwaukee: Pharmaceutical Review Publishing Company, 1904.*)

This volume is intended to describe with historical accuracy the men, scientific, semi-scientific and otherwise who frequented the court of Rudolph II, Emperor of Germany, and to portray the scenes to be witnessed there in the sixteenth century. The first chapters of the book are devoted to Dr. Dee, an Englishman of great erudition, who undoubtedly was the dupe of his associate and helper, Kelley, a forger and pretender. He seems to have been a religious enthusiast whose sincerity alone relieves his name from the imputation of great guile. The tale of the residence of Dee and Kelley in Prague and Cracow and the return of the former to England to end his days in honor as the Warden of Manchester College, and the downfall of the latter to end his days in prison and by torture are well told. The chapter on seeking the Philosopher's stone is exceedingly interesting. The *wit* of the unknown Westphalian alchemist to whom Rudolph II had sent a messenger to invite him to his court is worthy of reproduction. The emperor received the epigrammatic reply: "If I possess the Philosopher's stone I have no need of the emperor; if I do not possess it the emperor has no need of me." The descriptions given of the "magistery" of the Philosopher's stone are varied and interesting. We are informed that some alchemists believed that it would transmute one hundred times its weight of mercury into gold; Roger Bacon on the other hand claimed for it a multiplying power of one hundred thousand and Hollander of one million. Most alchemists believed that mercury was essential for transmutation into gold, but "Töpfer made the important discovery that gold could be made out of Jews. He had found by experiment that twenty-four Jews yield by proper treatment one-half ounce of gold, so that by repeating the process daily with 100 Jews, making due allowance for holy days, 624 ounces of gold could be made in twelve months." The story of Tycho Brahe and also of Kepler and others who found a hospitable refuge at the court of Rudolph, is interestingly told. The concluding chapters on "Medicine," "Magic and Sorcery," and the "Decline of the Follies of Science," are very suggestive. The author shows how astrology gave us astronomy, alchemy chemistry, and the search for the Philosopher's stone many inventions and mechanic arts. He traces the rise of mathematics, anatomy, botany, and kindred sciences to the stimulation of thought which followed the vain quest after the six follies of science, the Quadrature of the Circle, the Multiplication of the Cube, Perpetual Motion, Judicial Astrology, Alchemy, and Magic.

The style of the book is pleasing and the contents are suggestive and profitable to all who are interested in medicine and the allied sciences.

A Text-Book of Legal Medicine. By Frank Winthrop Draper, A. M., M. D., Professor of Legal Medicine in Harvard University; Medical Examiner for the County of Suffolk, Mass.; Medico-Legal Pathologist at the Boston City Hospital, etc. Fully illustrated. (*Philadelphia, New York, London: W. B. Saunders & Company, 1905.*)

The well-known unpreparedness of the general practitioner to appear in court and his common disinclination to do so have been the main reasons why the author has prepared this admirable text-book. According to him the medical witness should possess the following qualifications: 1. The faculty of accurately observing all things about him and of making full notes of what he sees. 2. A retentive memory. 3. Sincerity, candor and a mind unprejudiced. 4. A well-balanced temper that will remain unmoved under provocation. 5. A gift of expressing tersely and intelligibly what is in his mind. To this it seems proper to add the advice of Blizzard, "Be the plainest of men in the world in a court of justice; never harbor the thought that if you do not appear positive you must appear little or mean; give your evidence in as concise, plain, and clear a manner as possible. Be intelligent, candid and just, but never aim at appearing unnecessarily scientific. If you can, make your evidence a self-evident truth. Thus though the Court may at the time have too poor or too mean an opinion of your judgment, they must deem you an honest man."

With the exception of Toxicology and the Medical Jurisprudence of Insanity (which in the opinion of the author require a separate consideration), the book is a comprehensive text-book of legal medicine. It is carefully and painstakingly written and contains what the unfortunate medical witness should know. The chapter on Death by Electricity seems especially timely. We know of no similar work of its size which contains so much.

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CONTENTS.

	PAGE
A Contribution to the History of Medicine in Maryland During the Revolution. 1775–1779. By Walter R. Steiner, A. M., M. D.,	241
Situs Transversus and Atresia of the Pylorus. By H. M. Little, M. D., and H. F. Helmholz,	249
A Case of Congenital Urethral Stricture Associated with Hematuria and Symptoms Suggesting Renal Disease. By John W. Churchman, M. D.,	256
Synesthesia. By Henry Lee Smith, M. D.,	258
Correspondence. By A. Rose,	263
Proceedings of Societies:	
The Johns Hopkins Hospital Medical Society,	264
Analysis of 221 Cases of Typhoid Fever [Dr. Thompson];—Painful Heels [Dr. Baer];—Atheromatous Cyst of the Scrotum; Bladder Calculus in an Infant; Congenital Urethral Stricture; Traumatic Atrophy of the Testicle [Dr. Churchman].	
Notes on New Books,	265

A CONTRIBUTION TO THE HISTORY OF MEDICINE IN MARYLAND DURING THE REVOLUTION. 1775-1779.*

By Walter R. Steiner, A. M., M. D.,

Formerly House Medical Officer, The Johns Hopkins Hospital.

The Revolution found the colonies but ill prepared medically to carry on a long war, for instruments and medical supplies were very scarce and England could no longer be appealed to when more were desired. The dearth of these necessaries in war became more and more apparent as the Revolution continued, and the pathetic statements of the different army surgeons strike a tender spot in our hearts, even to-day. Who has not been touched by this sentence Morgan writes in a letter to Dr. John Warren of Boston: "I send you two (scalpels) in which case you want more, use a razor for an incision knife."[1] The mournful words of Dr. John Bartlett to Dr. Potts are even more affecting: "I have a handful of lint and two or three bandages and that is all. What in the name of wonder I am to do in case of an attack God only knows; without assistance, without instruments, without everything."[2]

In Maryland this lack of instruments and drugs was most kneely felt. The Council of Safety, on April 23, 1776, write to the Maryland Deputies in Congress that they have received the surgeons' instruments and delivered them safe to Dr. Wiesenthal,[3] but this supply was evidently not enough, for less than three months later we learn that Dr. Wiesenthal wants the instruments very much.[4] He wished them for distribution among the other regimental surgeons of the Mary-

* Read before the Johns Hopkins Hospital Historical Club, October 10, 1904.

[1] Packard, The History of Medicine in the United States. Phila., 1901, p. 302.

[2] Packard, op. cit., p. 300. Morgan at this time was director-general and chief physician to the army. Dr. Potts was the deputy director-general of the northern department and Dr. John Bartlett the physician and surgeon-general of the same department.

[3] Council of Safety, I, p. 370. This paper is based on a study of the Maryland Archives. Volumes XI, XII, XVI, and XXI of the Archives are designated in the foot-notes: Council of Safety, I, II, III, and IV.

[4] Council of Safety, II, p. 35.

land troops, for later he writes: "Chirurgical Instruments are not in my possession except a few Lancets, a Bullet forceps and some needles, as well as three small Catheters, having hitherto made use of my own instruments. The Capital Instruments are on board the Defense and in Annapolis."[6] Dr. Richard Tootel had, also, given to the Council a list of surgical instruments he desired, which was forwarded to the Maryland Deputies with the request that they be procured and sent down at the first opportunity.[6] When Dr. Michael Wallace resigned his position as Surgeon to the First Maryland Regiment, in 1777, he tells the Council of Safety, "I have a very elegant set of amputating Instruments, and some other surgical apparatus; these I would rather not sell, unless the Council of Safety may hereafter find great difficulty in procuring such articles."[7]

At the beginning of the Revolution the medical shop of a Baltimore loyalist, Dr. Alexander Stenhouse, materially increased Maryland's supply of drugs. The appraising of this "shop" was done by Dr. Wiesenthal, who found "the medicines are all of a good quality, and saleable in case they should not be wanted the price is less than what medicines at present sell for, and that is considerable." "I thought it was necessary to take the whole shop," he adds, "not only because the Drugs must be contained in something but more particular that they can be kept in proper order and regularity, since they must occasionally be divided there ought to be a proper repository for the whole."[8] "Some few drugs were wanting," he says, "of which we have too little, at least in some small space of time, (viz.) Jesuit's Bark, of which we have but 5 lbs., next opium and Spanish flyes."[9] The necessity for which remedies caused the Council a month later to order Dr. Wiesenthal to purchase for the use of the regular service of this province 30 lbs. Jesuit's Bark, 2 lbs. Cantharides, and 4 ozs. of Opium. One pound of Spunge was also desired.[10] The price paid Dr. Stenhouse for his "shop" was four hundred and thirty-eight pounds, three shillings, and two pence,[11] showing that he was, probably, liberally compensated. "Some necessary Surgeon instruments" were included in this purchase. In 1777 another loyalist, Dr. Patrick Kennedy, left Baltimore,—this time with French leave, and Colonel Gist writes he has left sundry medicines here which are much wanting in the Continental Army.[12] We hear nothing else about them so we imagine they were forthwith confiscated.

This need of medicines for the troops in the field gradually became most urgent. In October, 1776, General Smallwood had written from Philips Heights: "We want medicine much, none can be had here."[13] A month later, this lack of drugs was even more evident, and Pine tells Tilghman that he found "the sick in both the Regular and Flying Camp Maryland Troops without the least morsel of Physick of any sort, although a great many of them were in a very piteable condition." He had applied to Dr. John Morgan, the director-general and chief physician to the army, for some drugs, but was told that it was the State's duty to furnish her regimental surgeons with medicines, and none could be obtained from him. A letter from General Smallwood, subsequently, caused him to relent and tell Pine he could have some remedies if he would go from White Plains to Newark for them. The distance, however, was too great for him to make this trip and return before the term of enlistment of many of the Maryland troops should have expired.[14]

Notwithstanding, then, Maryland's scanty store, the Board of War requested the State early in the year following to furnish Dr. Samuel McKenzie, Director of the Hospital at Baltimore, with such medicine as he shall require. To this request Maryland generously complied, furnishing the abovementioned doctor with such medicines as they could possibly spare. They "sincerely wished it had been in their power to have done it more amply, but considering the number of sick in this State and their low stock of medicine they could not part with a larger quantity."[15] Six months later their stock was even more depleted, for we learn "medicines there are little or none in the country."[16] It was about this time that the physicians, practicing among the citizens of Maryland, so lacked medicinal resources that the State on at least two occasions sells them the desired drugs. For the Surgeon in charge of the Hospital at Annapolis is requested to "deliver one pound of Jallop for the use of some people, who are under Innoculation in Charles County,"[17] and, again, the same surgeon turns over to Dr. C. A. Warfield, of Anne Arundel County, "2 lb. P. Bark, ½ lb. Gum Camphor, 2 drachms of Opium, 2 oz. of Balsam Copaiba, ½ lb. Rad. Jal-

[6] Ibid, II, p. 300. The Defence was the provincial man-of-war.

[6] Ibid., II, p. 120. To this request Stone for the Deputies replied four days later: "We shall endeavour to procure the Instruments desired by yours of the 25th but they are not easily procured, the Demand for the continental army being great and many of the cutlers of this city having gone to Jersey with the militia" (Ibid., II, p. 146).

[7] Ibid., III, p. 183.

[8] Ibid., I, pp. 149-150.

[9] Ibid., I, p. 144.

[10] Ibid., I, p. 294.

[11] Ibid., I, p. 192. He was probably paid in currency, the pound currency being worth three dollars, thirty-three and a third cents.

[12] Ibid., III, p. 241. Dr. Henry Stevenson, of Baltimore, was, also, a prominent loyalist. Two casks of gunpowder were taken from him in 1776. The reason given for this was "as he has neither signed the Association or Enrollment, he stands in the light of an Enemy to America, and therefore it would be dangerous to trust so much Powder in his hands" (Ibid., I, p. 496).

[13] Ibid., II, p. 360.

[14] Ibid., II, p. 480.

[15] Ibid., III, pp. 151 and 152. February 22, 1777, is the date when McKenzie is spoken of as Director of the Continental Hospital at Baltimore. He must have resigned about April 3 of that year, for we then learn that Mr. John Griffith declined this office (Council of Safety, III, p. 198). Some one was greatly needed at this time to "purchase and furnish for the use of that Hospital, Rice, Indian Meal, Molasses and such other food for the sick," who were under inoculation there.

[16] Scharf, Hist. of Md., Balto., 1879, II, p. 315.

[17] Council of Safety, III, p. 189.

lop. 1 lb. Sal. Cathart., 5 lb. Calomel Prep., and ½ lb. Argent. Vir. for the use of those greatly distressed for want of Medicine."[18] Somewhat earlier Dr. William Murray is allowed to receive "half a Pound of Bark from this same source."[19]

This great scarcity of drugs, especially "Bark and a few other Capital Druggs essential for the Army and exceedingly wanted for the Use of the Country"[20] induced the State Council, in 1777, to consider fitting out an expedition to Havana to obtain them. With this end in view they wrote to Captain James Campbell, on May the first, asking him to make the journey.[21] His affairs, however, did not appear to permit him to undertake this matter for the public and Captain Conway was, finally, selected for this purpose. The following letter was accordingly written by Governor Johnson of Maryland to the Governor of Havana, and entrusted to Captain Conway's care:[22]

Annapolis in Maryland. Augt 8th, 1777.

Sir:—

I flatter myself the Occasion will apologize sufficiently for the Trouble I give your Excellency by this Letter. We are situated in a country where Drugs of various kinds are necessary and none more so in some Cases, than Flies, or in many, than Peruvian Bark. Since our Connection with England has ceased and our intercourse with Europe is interrupted and almost cut off by the British cruisers we must Enquire in other Places for such essential Articles as we have not amongst ourselves. I have therefore, ignorant of what may be either suitable or admissable at the Havanna, sent Capt. Conway in Hopes of getting a Quantity of Flies and Bark for the use of the Troops; but with Directions not to dispose of anything without your Excellency's Permission. I hope the subjects of his most Catholic Majesty and those of the United States, may be mutually benefitted by a generous and fair Commerce and shall be happy if this Incident should lead to an Acquaintance and Confidence between those in your Department and those over whom I have the Honor to preside. If I request too much in soliciting leave for Capt. Conway to sell his Cargoe and purchase Drugs and a little Salt, I shall be exceedingly obliged by your giving him credit with some of your Merchants for about two thousand Pounds of Bark and one hundred pounds of Flies, and shall be careful to cause a just Remittance to be made. I am Sir with great Truth & Respect

Yr Excys most obt Servt

Governor of the Havanna.

The essence of the instructions to Conway is largely contained in the above letter. He was to proceed in the Molly to Havana, and it was stated that the Flies probably would "cost less than 5/ or 6/ Sterling and the Bark under 5/ Sterlg p l. perhaps much under." "You must expend," the latter continues, "as little as possible on the vessel whilst abroad, as you go armed you'll use your own discretion altogether as to attacking any Enemy Vessel and if you should be so fortunate as to take a prize, send her if the Chance is equally good for her getting into Port, to Mr. Harrison at Martinique with Directions to transmit Accounts as soon as possible that the men may be paid here when you arrive again upon the Coast, if convenient, run into one of the Inletts, Sinnepuxent we would prefer, which would be the best Port too for a Prize on all accounts if you send any to the Continent you will enquire in any Port you may go what may be had and what of our Produce may be disposed there, and the Prices for the advantage of our Trader as well as the public."[23] The Council, subsequently, in another letter, doubts "whether Conway can get out; from the last we heard from Virginia, the Men of War still continue at & about the Capes." They add, if Colonel Hooe thinks "it prudent to risk, advise the Captain so, if not, we do not intend his Orders for Sailing as absolute."[24]

Before Conway started out the instructions were changed and he was ordered "to proceed to the Moale and there dispose of his Cargoe and purchase there Bark if to be had on good Termes." If not, he was to go to Havana.[25] Unfortunately we do not know where Conway went, but we are told later that "Doct. Johnson is desired to sell four hundred Pounds weight of the Bark lately imported in Captain Conway at four Pounds per pound and to receive the money and pay it into the Treasury not disposing of more to any one private family than two Pounds or to any Practicing Phisician more than eight Pounds."[26] Doctor Johnson is, also, elsewhere requested to let "Doct. Craigg have 250 lbs. Bark."[27]

Besides these deficiencies, there were too few regimental surgeons and too frequently those who held office were lamentably incapable. Captain Thomas writes to the Council from Harlem September 4, 1776: "We have now and have had for some time a number of our men sick, a number very ill. I have had from fifteen to twenty of my men extremely ill and have not yet been able to procure them the least assistance. The Province have but two Surgeons here, one of them very ill, and none can be procured here. From the best authority I can assure you we have at this time near two hundred men unfit for duty and most of them without any assistance from the Doctor."[28] He had also written to the Maryland Deputies, who, thereupon, desire the Council to send, "if it be in their power a skilful and attentive person who should have the immediate care of the Independent companies. We have requested Dr. Bond, they state, to recommend such a one that we may propose him to congress for this purpose, but from the Doctor's answer we almost despair of finding a suitable person here."[29] More surgeons were finally

[18] Ibid., III, p. 291.
[19] Ibid., III, p. 25.
[20] Ibid., III, p. 235.
[21] Ibid., III, pp. 235-236. Captain Campbell at one time commanded Maryland's naval forces in the neighborhood of Hooper's Straits and Tangier Sound (Scharf, Hist. of Md., Balto., 1879, II, p. 301).
[22] Council of Safety, III, pp. 328-329.
[23] Ibid., III, p. 327.
[24] Ibid., III, p. 330.
[25] Ibid., III, pp. 331-332.
[26] Ibid., IV, p. 7.
[27] Ibid., III, p. 547.
[28] Ibid., II, p. 256.
[29] Ibid., II, p. 292.

appointed and "if they are all gone up," the Council declares, "there can be no just cause of Complaint."[30] General Smallwood about two weeks later, however, says: "We have upwards of Three Hundred Officers and Soldiers of the Maryland Regulars very sick . . . and I am sorry to say its shocking to Humanity to have no more Care taken of them."[31] He later, again, speaks of the suffering, which was due to the great neglect of the sick. The Directors of the General Hospital, he claimed, were "extremely remiss and inattentive to the well being and comfort of these unhappy men." He consequently had all of his "sick removed to a comfortable house in the country and had supplied them with only the common rations as even that was preferable to ordinary Hospital fare."[32] He continues: "One good seasoned and well trained soldier recovered to health is worth a dozen new recruits, and is often easier recovered than to get a recruit, exclusive of which, this neglect is very discouraging to the soldiery and must injure the service upon the new enlistments."

Thomas Stone, a member of Congress from Maryland, writes, on September 30, 1776, from Philadelphia: "Surgeons are much wanted in Camp but where proper ones will be procured I know not."[33] While early in the next year Thomas Johnson begs the Council of Safety to send "us in Frederick a skilful physician it will be well worth while, we are badly off, and the people who go from the little care taken of their countrymen, are very apprehensive of fatal sickness, indeed I fear that their scanty clothing will subject them to severe pleurisies."[34]

During the war State Hospitals were established at Baltimore and Annapolis. The former had a somewhat checkered existence, for it was only organized six months (from May to December, 1776) when it was given up and the sick were attended at the fort, at Whetstone Point. After nine months it was again instituted and continued from September, 1777, until March, 1778. It was revived, again, in September, 1178, and was located at the Continental Hospital until it was removed, two months later, to the fort at Whetstone Point.[35]

[30] Ibid., II, p. 304.

[31] Ibid., II, p. 343.

[32] Ibid., II, p. 360. It is well to quote Dr. Toner in this connection. "Officers of all grades in the various departments were in the habit of writing exaggerated complaints to the Council of Safety and to Congress, and because sympathy could most certainly be excited in favor of the soldier, the hospital department was taken as the theme for denunciation, and accused of most cruel neglect, and in some cases of absolute inhumanity, and the gravest charges brought against the surgeons." He then quotes General Smallwood's letter as an example, from which I have taken the above extract (Toner, Medical Men of the Revolution. Phila., 1876, p. 63).

[33] Council of Safety, II, p. 312.

[34] Ibid., III, p. 36.

[35] Ibid., IV, p. 245. Congress resolved, October 6, 1776, that "no regimental hospital be for the future allowed in the neighborhood of the general hospital" (Toner, Medical Men of the Revolution. Phila., 1876, p. 78), so when the general hospital was given up Dr. Wiesenthal re-established the regimental hospital in the former's building, having already treated "several sailors from the Galleys there." Besides a previous note I have been able to obtain no information concerning this General or Continental Hospital at Baltimore.

The Maryland Archives give many interesting items concerning the hospitals. We learn that at least five women (Eleanor Kirby,[36] Eliza Sharpe,[37] "Philis" Waterland,[38] Catharine Nixon,[39] and Catharine Minsky[40]) served as nurses, and John Amber or Aubber[41] was also employed in some official capacity—possibly as an orderly, for we know Philip Sulivan,[42] Richard Gee, Daniel Hall, and Joshua Lester[43] were enrolled as Orderlies in the Hospital. While Daniel Barnet[44] is mentioned as Orderly to the Flying Hospital, during the months of September and October, 1778, and Hugh Doyl, Richard Carter, and Neal Peacock[45] are spoken of as Orderlies to or for the sick. We, also, learn from this same source that the State liberally looked after the wants of the Hospital, 200 pounds,[46] 100 pounds,[47] and other sums being appropriated for its use. At one time David Kerr is paid "two shillings and six Pence for Vinegar for the Hospital,"[48] and, at another, William Lavely receives five pounds, eleven shillings, and a penny for 1010 pounds of bread for the Baltimore Hospital.[49] The supplies were procured by the quartermasters, who served under the physicians in charge. Joseph Marbury seems to have been the first of these quartermasters to hold office.[50] When the hospital was re-established in 1777 John Hart received the appointment on September 5,[51] but continued in office only until November 5, 1777, when Samuel Gerrock succeeded him.[52] Shortly thereafter the Council, thinking Gerrock's accounts more than they expected, though possibly very just, requested Dr. Gale, in charge at the hospital, to send them a list of those who are in the hospital, "noting what Service they belong to, and whether they are likely to be again fit for Service." They do this as the sum expended may be owing, "in some measure, to the Peoples remaining there who might be returned to their Duty or of others who are not likely to be fit for Duty."[53] On Novem-

[36] Council of Safety, II, p. 245.

[37] Ibid., II, p. 257.

[38] Ibid., II, p. 257 and p. 321.

[39] Ibid., II, p. 298.

[40] Ibid., II, p. 317.

[41] Ibid., II, pp. 252 and 313.

[42] Md. Archives, Muster Rolls, p. 392.

[43] Ibid., p. 391.

[44] Ibid., p. 308.

[45] Ibid., pp. 306 and 307.

[46] Council of Safety, III, p. 421.

[47] Ibid., IV, p. 271.

[48] Ibid., II, p. 134.

[49] Ibid., II, p. 187.

[50] Ibid., I, p. 241. Marbury was quartermaster of the First Regiment and seems to have acted in a like capacity at the General Hospital.

[51] Ibid., III, p. 363.

[52] Ibid., III, p. 409.

[53] Ibid., III, p. 446. On another occasion (Ibid., IV, p. 235) Gerrock seems to have procured eleven barrels of powder on false pretenses, which he was ordered to return. If he would not, Luther Martin was to sue him for them.

ber 5, 1778, Gerrock was displaced by Lieutenant Samuel Sadler, "who was much more conveniently situated."[54] Medical attendance was furnished by surgeons acting under the directions of Dr. Wiesenthal, and we know that Doctors William A. Dashiell, Michael Wallace, and George Gale were numbered among those who served there. When Dr. Wiesenthal went to Virginia in May, 1776, Dr. John Coulter seems to have taken his place and had sole charge, for which service he was paid 46 shillings some months later.[55] He evidently gave satisfaction, for when Dr. Wiesenthal made a second journey, to look after the Maryland troops, Major Smith suggests that if it would be agreeable to the Council he would prefer to apply to Dr. Coulter for medical assistance. Smith generously adds: "Coulter will do it as cheap as any one, being at the same time the most skillful."[56] A subsequent item of 46 shillings, paid to Dr. Coulter for attending the hospital, would seem to show that he was again selected to look after the sick there during Dr. Wiesenthal's absence.[57]

The removal of the hospital to the fort at Whetstone Point was the subject of much discussion, after it had been carried into effect. It was done by Major Nathaniel Smith and the State subsequently approved of the change of location, for we read: "We much approve your Removal of the Hospital and the good effect it has had ought to silence all objections; we would have the Sick continued at the Point; unless Circumstances should hereafter make it prudent to remove them." There must have been some complaint against the physician in charge as the letter continues: "It is for the Sake of the Sick only that we employ a Doctor, Quartermaster or Nurse, the Doctor must attend his Duty or we must get another." A nurse was evidently employed in the town, but was not needed at the fort, as the letter states: "We dont imagine any pay will be expected for a Nurse in town when there was no sick there; the Woman you have employed and who has done a real public Service ought to be paid by the Public."[58] Major Smith's action, however, was somewhat high-handed, as he did not consult Dr. Wiesenthal, which caused the latter to have a bitter correspondence with Governor Johnson and Major Smith over the matter. It seems that when the "sickly season" came on in September, 1778, and when a soldier died at the fort of "some Putrid Complaint," Dr. Wiesenthal recommended that the sick be removed to the Continental Hospital, which was nearly empty. He also ordered the foul straw to be taken away from the beds there. Shortly thereafter, while Wiesenthal was away, on a trip to St. Mary's County, to amputate Colonel Forrest's thigh, Smith ordered all the sick to be removed to the fort at Whetstone Point, without even consulting the attending surgeon. He, also, characterized the State Hospital as a horse stable, chiefly on account of its foul straw (which had not been changed, as Wiesenthal ordered) and its broken windows.

[54] Ibid., IV, p. 230.
[55] Ibid., II, p. 62.
[56] Ibid., II, p. 151.
[57] Ibid., II, p. 220.
[58] Ibid., IV, p. 230.

Upon Wiesenthal's return he writes a letter to Governor Johnson, recounting that lack of fresh straw is due to the quartermaster not furnishing any and that Smith is partly to blame as he could have furnished some from his farm. The broken windows were not a detriment to the State Hospital, Wiesenthal claims, as it was summer time. "Upon the whole," he adds, "as I presume that the Doctor is the principal man in Hospital Affairs & its Direction, and that the Quarter Master, is his Assistant, to procure those things which the Doctor orders, I do not know what Business the Comander has with him at any Rate, except where faults are comitted and then he is to assist, to have those faults remedied in a proper manner, the quartermaster is to receive Orders from the Doctor for everything he is to furnish in his handwriting and have his Acc^{ts} again acknowledged & signed before he can settle his Affairs."

"As the Doctor prescribes the Diet according to the Nature of the Disorder some will receive full Diet, others half Diet, some one thing some another and as a Diet is not always pleasing to obstrepulous Soldiers they will make Complaints, if then the Comander is so weak as to listen to their Complaints as valid, and so hasty as to conclude without proper Inquiry, he will do great mischief. I mention this as an example which has happened, when some sugar was ordered on particular occasion, & which being withdrawn when that was over it being so disagreeable to be deprived of so sweet a thing, that they grumbled and preferrd general Complaints, as if they were stinted, whereupon the quarter Master was ready to give what they wanted rather than to be exclaimed aga^{t} untill I thought it requisite to give him positive Orders to the Contrary. Nevertheles such things will gradually breed bickerings and at last open Complaints, for want only of proper limits in every ones Department."

He finally begs that Johnson will direct the Major to "Consult me in Cases of Sickness of the Soldiers and to follow my Directions in hospital Matters, as likewise to desire the quarter Master of the Sick to apply to me properly."[59]

Wiesenthal's letter to Smith tells him plainly that, while the fort will do to treat trifling disorders in, it is an unfit place for a hospital as it is "surrounded with Water in itself sickly." This must make it "more difficult for People already sick to recover And I beg that you will represent to your Mind a Danger which you little thought of, I mean the impurity of the Air, when the Patients are obliged to swallow the Effluvia arising from their diseas'd Bodys which on Account of the Lowness of the Building can not properly rise and be ventilated, this will inevitably turn slight disorders into putrid and dangerous ones, Nay in case any Person should be taken with such a Complaint, (as we have had many) he must unavoidably infect the Rest, nay even the healthy for Instance if Poor who lately died had unfortunately been at that place it would most probably have furnished a dreadful Lesson of the Truth. For these Reasons to avoid any Infections Hospitals have generally been estab-

[59] Ibid., IV, pp. 243-246.

lished quite out of the Way and I believe you stand singly to be so assidnous to place even in the midst amongst you."

Wiesenthal, also, shows Smith in this letter how awkward it would be to send sick soldiers to the fort "to crowd the place," as there was no Continental Hospital, at present, in Baltimore.[59]

The Archives do not state when the hospital at Annapolis was established. Probably it was in July, 1776, in which month Dr. Richard Tootel was appointed Surgeon to Colonel Hall's Battalion of Militia.[61] It appears that he then assumed charge of the hospital. Thomas Henry Howard was appointed his surgeon's mate at this time [62] and William Gerwood, subsequently, received the same berth.[63] On December 17, 1776, Beriah Maybury was made quartermaster.[64] He was able to provide for the hospital efficiently, as the State responded well to requests for supplies. Bedding,[65] wine, spirits, and other necessaries out of the public store [66] are mentioned as being furnished, and various sums of money were appropriated for its use. On two occasions ten and thirty pounds of candles [67 68] were doled out to Captain Maybury, the quartermaster, for the use of the hospital. Infectious diseases were not treated there, and Dr. Tootel is requested, on September 17, 1776, to remove all such cases and have them nursed in private houses.[69] In the previous month Colonel Hall's Battalion had received its marching orders, which caused the doctor to protest against going on account of his age, bad health, and particularly the season of the year. "I could scarce think," he says, "of leaving home and between three and four hundred a year, arising from my practice of Physick and other advantages, to move into another province and leave my Family, consisting of a Wife, a Daughter and a small son for whom I have the most tender affection, and who in my absence must inevitably suffer, to embrace a surgeon's place, which pay would scarce defray my expenses as I should be oblig'd to travel with a servant and Horses, and perhaps be ordered by the Surgeon General to what department he pleased.

"I have attended the sick soldiers with the greatest assiduity and care and I believe I have given general satisfaction both to the officers and soldiers. I have had great fatigue and trouble regulating the Military Hospital shop and compounding various Medicines from the gross materials, which was acting beyond my line of office It being my duty only to prescribe for the sick, the Medicines ought to have been delivered to me ready for prescription. The Hospital is now filled with sick soldiers which I am ready to attend, and likewise the train of Artillery and any other troops that might be stationed in this city. I should be sorry that the Battalion should suffer, from my not marching with them and really as I'm circumstanced at present that is impracticable." [70]

The Council appears to have been touched by this appeal and Dr. Tootel was permitted to remain at Annapolis.[71]

In 1777 the hospital burnt down [72] and the building hereafter used was apparently not State property as we learn James Williams was paid eighty-five pounds on February 17, 1779, for one year's rent of the hospital.[73]

From "returns" we find the following diseases affected the Maryland troops during the Revolution: putrid fever, inflammatory fever, intermittent fever, "peupneumony," bilious fever, rheumatism, diarrhœa, flux, jaundice,[74] and that dreadful scourge small-pox. This last disease was always with the army at some point, though Washington's firm belief in inoculation, which he caused to be carried into practice, greatly lessened its dread mortality. A number of outbreaks of this disease occurred in Maryland. In May, 1776, Colonel Ware writes the Council of Safety that he has just been "informed by Dr. Wiesenthal that small-pox prevales in several parts of Baltimore and fears the command might take the infection." He was advised by the doctor "to be enockolated emediately as a person of my age must be in great danger who takes it in the natural way." He, consequently, thought it his duty to state the matter to the Council and wait their instructions.[75] To this the Council replied and cheerfully absolved themselves of all responsibility by saying: "We leave Colonel Ware entirely at large on the Point of Inoculation. We think it the safest method of taking the Small Pox, but would have him judge of the Risque." [76]

In July of the same year small-pox broke out among the troops under Lieutenant Bracco's command at Port Tobacco. He desires Tilghman to let him know in what manner to act, whether "emediately to inoculate the remainder of the men or remove them out of the way." The latter he thinks would be of no effect as the man "who communicated the infection was a day and night in company with all the Soldiers here, some combed his hair and others slept with him." He was thought to have been previously inoculated by Dr. Browne "who had the care of the fellow." [77] As only four of Bracco's men had had the disease, the Council advised all the others to be immediately inoculated. They desired Bracco to apply to Dr. Craig for this purpose, making the best bargain possible with him. They, finally, add that all expenses will be paid,[78] and

[59] Ibid., IV, pp. 246-247.
[61] Ibid., II, p. 15. He had applied for the place but two days before his appointment (Council of Safety, II, p. 7).
[62] Ibid., II, p. 15.
[63] Ibid., II, p. 394.
[64] Ibid., II, p. 534.
[65] Ibid., II, p. 174.
[66] Ibid., II, p. 534.
[67] Ibid., IV, p. 256.
[68] Ibid., IV, p. 112.
[69] Ibid., II, p. 276.
[70] Ibid., II, pp. 217-218.
[71] Eleven days later David Murrow was appointed Surgeon of Colonel Hall's Battalion (Council of Safety, II, p. 245).
[72] Cordell, The Medical Annals of Maryland, 1903, p. 659.
[73] Council of Safety, IV, p. 305.
[74] Md. Archives, Muster Rolls, pp. 619 and 620.
[75] Council of Safety, I, p. 399.
[76] Ibid., I, p. 403.
[77] Ibid., II, p. 125.
[78] Ibid., I, p. 531.

later learn that the men are all getting through the small-pox as well as can be expected, in a letter Bracco writes, asking for a sum of money to defray the expenses. "I have expended almost all my own cash," he says, "and when that is gone we may whistle for provision until we can get a fresh supply. The People here follow a very good rule, not trust us farther than they can see us."[79] He was subsequently allowed one hundred pounds for this purpose.[80] Again, in December, 1776, there is a note in the Archives concerning a man on board Captain Conway's sloop with the small-pox. He belonged to St. Mary's county and wished to return there. The Council, consequently, wrote to Captain Ignatius Taylor of that county, inquiring of him if he was inoculating in his house and, if so, asking him to take the sick man in. If he was not inoculating, they desired him to get the man into some house that has the small-pox or into some house where the family have had that disease.[81]

Early in the next year Surgeon Barton Tabbs writes: "The soldiers in Lawrence's Barracks are breaking out fast with the Small Pox. I am told they have all had it except eight or ten. I think it will be the best way to move them to the poor House and inoculate them immediately. If they are suffered to remain in the Barracks and take it in the natural way, the greater part will certainly be lost. There has been five sent up within this two days, and I don't expect above one will be saved. There can be nothing else expected considering their way of living. Those who were inoculated are in a very good way, but the poor fellows who has it in the natural way are in the most horrid situation."[82] Two months later Thomas Smyth, Jr., informs the Governor that "we are preparing at Chestertown for the inoculation of our men," and mentions the great lack of blankets and other necessaries. He, also, states that the people of Chestertown were much opposed to having the troops inoculated there, fearing lest it might spread the disease, which had not been seen among them for many years.[83] We are also, elsewhere, informed that small-pox had affected some of Colonel Richardson's Regiment at Cambridge, in July, 1777.[84]

Two interesting references to invalided soldiers are to be found in the Archives. The first soldier was James O'Hara, "who had the misfortune, before the departure of his Battalion from the province, to take cold standing centry at night which brought on an universal Eresypelas from head to foot, the vesications common in that Disorder discharged a humour so sharp that in few days he was all over deprived of his skin, his eyes likewise suffered to that Degree as to deprive him of his sight." He finally recovered but his sight was permanently lost. Wiesenthal writes an interesting letter on his behalf to Jenifer, the President of the Maryland Convention.[85] The second soldier, Robert Hurdle, was a member of Captain Truman's Company of the Sixth Maryland Regiment. He had sore legs and was consequently discharged, "being represented by Doct. Wallace and Doct^{r} Johnson as not likely in a long time if at all to become fit for the Service."[86]

On July 23, 1777, Eddis writes from Annapolis to Eden that "the Mortality which has prevailed among the Provincial Troops is incredible. A vast number of those raised in Maryland brought back with them the Camp fever & died prodigiously fast the Church yard, the back of the Poor House and a Piece of Land which is enclosed in the Folly, are crowded with melancholy proofs of Calamity."[87] I can find no other note concerning the death-rate of the Maryland troops.

The surgeon's pay was fifteen pounds per month, generally, while that of his assistant or mate amounted to seven pounds and ten shillings.[88] These rates were not fixed, however, for some of the surgeons appear to have been paid a lump sum per year,[89] and others were certainly paid less than the above amounts. In 1777, Bruce writes to Governor Johnson that he had informed Dr. Buchanan, Johnson had sent for his commission as surgeon. Whereupon Buchanan asked what his pay would be. Bruce replied that he believed it to be about 30 or 33 dollars a month. Thereupon Buchanan told him he would not go under fifteen pounds, though Bruce informed him it would have been proper in him to have known the pay before he asked for the berth. Bruce then states that "Mr. Thomas Charleton wished to go out as a surgeon, and though he did not know anything of Mr. Charleton's abilities yet they must be poor if they are not equal to Doct. Buchanan."[90]

The surgeons were appointed, as a rule, by the State, at

[79] Ibid., I, p. 543.

[80] Ibid., I, p. 554. Ten days later, as Bracco had exhausted both money and credit, he writes for a further sum for their subsistence. Unless this is sent he "shall be obliged to suffer the men to disperse and let each man look out for himself." He thought "as the small-pox was very favorable ten days from this we shall be able to do duty" (Ibid., II, p. 59).

[81] Ibid., II, p. 528.

[82] Ibid., III, p. 112.

[83] Ibid., III, p. 204.

[84] Ibid., III, p. 309.

[85] Ibid., II, p. 513. The State did not leave him destitute. He was discharged Aug. 5, 1777, but was allowed to draw rations while he continued at Annapolis and until further directions (Ibid., III, p. 324). In 1779 the State paid him 75 pounds and allowed him a pair of shoes and a pair of overalls (Ibid., IV, p. 494).

[86] Ibid., III, p. 547. Three others are mentioned as being discharged because they were invalids, one because he was "subject to fits," one had the spleen, one a "Dropsical Complaint," and still another had lost the use of his arm (Ibid., III, pp. 206, 305, 308, 450, 453, and 463). John Woodfield was given a furlough, which was twice extended, as the doctors thought "Country Air would be of service for him" (Ibid., IV, pp. 237, 269, and 316).

[87] Scharf, loc. cit.

[88] Thacher gives the pay as 33 and 18 dollars per month, respectively (Thacher, Military Journal, Boston, 1824, p. 73), while Scharf says it was 40 and 20 dollars (Scharf, Hist. of Md., Balto., 1879, II, p. 190). Council of Safety, I, pp. 22 and 421; II, pp. 336, 514, 553; III, pp. 130 and 503.

[89] Council of Safety, I, p. 467.

[90] Ibid., III, p. 33.

times by those in command with or without the State's subsequent confirmation.[91] Dr. Wiesenthal appears to have had some supervision over these appointments. Barrister Carrol in 1776 says: "I mentioned to Wiesenthal that he might have occasion for some assistants & there were many young gentlemen that offered themselves. We expected he would examine them," Carrol says, "and pitch on such as he thought best qualified. This he agreed to do, I think therefore that it may not be improper to send him the names of such as stand on the list."[92] Some two years later, Dr. Wiesenthal informs us: "I have all along contrived a Medical School to bring up young Surgeons for Military Service and in which I have the Satisfaction to have allready succeeded, instead of such, which after their hardly finish'd Apprentiship set up and act the wise Doctor with all the Arrogance at the expense of the patient."[93]

In this connection three letters of recommendation of young surgeons are of interest. The first one is by Dr. Wiesenthal and states that "Dr. Andrew Porter, having been a candidate for a Surgeons place on the Surgeons list for some time, is now willing to go as such in a Battalion going to the Flying Camp. His abilities for that station are such that can recommend him."[94] The second letter is from Dr. Thomas Gantt and refers to the candidacy of Mr. Thomas N. Stockett. "Having lived with Mr. Stockett," he states, "for four or five years past, the greater part of which time he applied himself to the study of Physick; and since my leaving that place, have had frequent opportunities of being acquainted with his method of practice; think him sufficiently qualified to act in that character."[95] The third is written by Dr. W. H. Jenifer and concerns William Marshall, who had served an apprenticeship of three years with him. Marshall, rather than not go into the army, had accepted an ensigncy, offered him by Colonel Stone, but as he had applied himself to the study of medicine and "by which he proposed in future to live," desired a surgeon-mateship. Dr. Jenifer adds: "I can assure you of his being assiduous and well qualified to fill that department."[96] David Morrow was, also, a candidate for a place in the medical service, and hearing nothing from the Council, though he had sent them a letter of recommendation from Doctors Cadwalader, Bond, and Shippen of Philadelphia, writes anxiously to know if he has gotten an appointment. He, also, desired the letter of recommendation to be returned, as it will cost him some trouble to obtain a second.[97] Dr. Wiesenthal, also, elsewhere refers to the candidacies of David Finlay, John Dorsey, and John Johnson of Frederick County.[98]

I regret that my material on hand does not suffice to give sketches of the prominent surgeons of the Maryland troops during the war. Many of them did, also, excellent work for the State on important committees, and not a few served her in other legislative capacities. Much information will be found in Dr. Cordell's recent book and in Dr. Quinan's writings. There is one man, however, I should like to mention, though his career has been carefully studied by Doctors Cordell[99] and Piper.[100] I refer to Dr. Charles Frederick Wiesenthal, who was born in Prussia in 1726. His interest in the organization of an army medical department in Maryland and his thorough knowledge of the management of such departments in both Prussia and England[101] caused him naturally to assume charge of medical matters in this State, at the onset of the war.

In his plan he would have a garrison or regimental hospital when the troops are in garrison and a moving or flying hospital when the troops take the field. This latter was to be placed in the rear of the army, on the next plantation. Besides these he would erect another hospital called the fixed hospital for the treatment of the wounded and the more chronic cases. The bedding and also the sundry articles of diet for this hospital were to be furnished by a commissary, while a Physician or Surgeon-General or Director-in-Chief would have the whole supervision of it. In this hospital a medicinal shop was to be located with a proper person for preparing the medicines, under the direction of the Surgeon-General. The latter was to "procure those medicines from time to time which become deficient (if to be had)."[102] I have previously shown in this paper several instances of the trust and confidence the Council of Safety reposed in him. He was made a member of the Baltimore Committee of Observation in January, 1775,[103] and towards the close of that year appointed supervisor of the manufacture of saltpetre for Baltimore county.[104] He later became examiner of candidates (as I have shown) for places in the medical service, medical purveyor and surgeon to the First Maryland Battalion. This last office he received March 2, 1776.[105] It was not the place he designed for himself as he wished to become the Surgeon-General of Maryland, but then there was no choosing, so he cheerfully accepted this office. He hoped for the above title later and seemed to have acted in the capacity of this position when he merely held the office of surgeon.

[91] This was the case with Dr. Samuel Y. Keene, who was appointed surgeon's mate by General Greene, and, though the State did not confirm this appointment, yet Keene continued to serve in the capacity of this position until the end of the war (see Muster Rolls, p. 478).

[92] Council of Safety, I, p. 172.

[93] Ibid., IV, p. 246.

[94] Ibid., II, p. 261.

[95] Ibid., II, p. 286.

[96] Ibid, III, p. 184.

[97] Ibid., II, p. 132.

[98] Ibid., II, p. 231.

[99] Cordell, Charles Frederick Wiesenthal, Medicinæ Practicus, the Father of the Medical Profession of Baltimore. Johns Hopkins Hosp. Bull., 1900, XI, pp. 170-174.

[100] Piper, Memoir of Dr. Charles Frederick Wiesenthal, 1900, p. 18.

[101] Council of Safety, I, pp. 144-145.

[102] Ibid., I, p. 321.

[103] Scharf, op. cit., II, p. 172.

[104] Cordell, op. cit. in Johns Hopkins Hosp. Bull., 1900, XI, p. 171.

[105] Council of Safety, I, p. 197.

For he then had the care and management of the State Hospital in Baltimore. He, also, had medical supervision of the troops from this State and the marines from the ship Defence; he had likewise fitted out the Defence with medicines, and twice furnished her with a surgeon in the absence of her own.[106] According to Dr. Quinan's manuscript, he received his wished-for office the next year, 1777, with a salary of thirty-five shillings per day, without rations.[107]

The ability he showed in the formulation and development of his subsequently adopted plan for an army medical department in Maryland and the skill he exhibited in the plan's execution merit for him long remembrance in this State by a grateful people.

[106] Ibid., II, p. 13.

[107] Dr. Tootel, in charge of the hospital at Annapolis, appears to have been like a thorn in the flesh and not much love was lost between him and Dr. Wiesenthal. On August 14, 1776, Wiesenthal thought himself superseded by Dr. Tootel and consequently discharged from any provincial employment, as the latter doctor was appointed surgeon to Colonel Hall's battalion of militia (then ordered to be stationed at Annapolis and Baltimore in place of Colonel Smallwood's battalion) and acted at the same time as director (Council of Safety, II, p. 202). Such was not the case, though, and everything continued serene until Dr. Tootel wrote Wiesenthal about one month later, saying the Council of Safety desired him to turn over to Tootel all the medicines, shop furniture, etc., belonging to the Province. The impracticability of this order Wiesenthal well shows, as a removal of the medicine shop could only be attended with manifest loss and great trouble. Besides, the Baltimore Hospital was just as crowded as the one at Annapolis and the former was the safest for the repository if any disturbance should happen in the Province. Then, too, the Maryland navy had been supplied with medicines from the Baltimore hospital from time to time. Wiesenthal elsewhere speaks of Tootel's extravagant invoice of medicines once sent him, of which even the whole city of Philadelphia could not have furnished half. A retrenchment of Tootel's prescriptions to the present situation of affairs was needed (Council of Safety, II, p. 299).

SITUS TRANSVERSUS AND ATRESIA OF THE PYLORUS.

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The mother of the child under consideration was a white woman, aged 33 years, of excellent family and personal history. She had been married thirteen years and after one child at term had had four miscarriages, one each year following, the first at six months, the remaining three at three to four months.

At the time of the first miscarriage she had been infected, and since that time had suffered from severe pain in the back, worse at her menstrual periods.

She first entered the hospital in August, 1903, when a chronic hydrosalpinx was removed, and the uterus, which was found retroposed and adherent, was freed and suspended to the anterior abdominal wall.

She became pregnant soon after her discharge, and menstruated last on December 19, 1903.

She re-entered the hospital on July 29, 1904. Her pregnancy had so far been quite normal. Shortly after her admission her abdomen began to increase markedly in circumference and the uterine tumor became so tense as to suggest tetanic contraction of the organ.

Labor pains began on September 15 and continued irregularly until September 19, when her child was born. There was an enormous amount of amniotic fluid, estimated at about 5 to 7 liters.

The child was a male, 48 cm. long, and weighed 2350 grams. The measurements of its head were: O. M., 13; O. F., 10.5; S. O. B., 9; B. P., 9.25; B. T., 8.25. The placenta weighed 525 gms., and was macroscopically and microscopically normal.

The child was slightly asphyxiated, but cried on slight stimulation. It had a peculiar appearance. The body still showed lanugo hairs and the facies was that of an infant that had become markedly emaciated. The eyes were small and sunken. Its cry was feeble. Its temperature at birth was 95°.

Shortly after birth it vomited about 20 to 30 cc. of greyish fluid, resembling amniotic fluid.

19/IX, 1st day. It was given small amounts (4-5 cc.) of water during the morning and afternoon. Was put to breast at 5 and 8 p. m.; during the night at 10 p. m. and 2 and 6 a. m. Given 15 cc. of a mixture of cream and whey (F 1%—S 7%—P .98%). Vomited a large amount at 6 a. m.

20/IX, 2d day. Put to breast for 15 minutes every 3 hours. Passed a small amount of dark meconium. Fed at night as before, and vomited feedings. Temperature still subnormal, 96.8°-97°. Has lost 60 gms. since birth.

21/IX, 3d day. Child restless. Bowels moved twice. Nursing supplemented with special prescription (F 1%—S 7%—P .98%). Vomited portions of feedings. Temperature still subnormal. Superficial veins of abdomen distended. Has lost 160 gms. since birth.

22/IX, 4th day. Condition somewhat better. Still losing weight; total loss thus far 218 gms. Temperature still subnormal. Bowels moved once—green meconium.

23/IX, 5th day. Mother's milk plentiful. Child vomited after each nursing. Gastric lavage at 8 p. m. and 10 p. m. All milk left in stomach at first, present at second washing. Bowels moved once—light green meconium. Temperature still subnormal. Loss of weight to date, 257 gms.

24/IX, 6th day. Bowels not moved. No urine voided. Temperature lower than on previous days. Gastric lavage in evening, followed by 10 cc. of castor oil. Part of oil vomited. S. S. enema given.

25/IX, 7th day. Small amount of green meconium carried away with the enema, and about an hour later the child passed a small amount of blood-tinged mucus. Lavage showed the presence of the castor oil in the stomach.

A diagnosis of complete obstruction of the pylorus or upper portion of the duodenum was based on the following considerations:

1. The vomiting of the large amount of amniotic fluid shortly after birth.
2. Recurrence of the vomiting not regularly after the ingestion of small amounts of fluids, but as soon as approximately 20 to 30 cc. had been given.
3. The presence in the stomach of entire amount of a feeding (15-20 cc.) when the stomach was washed out some two hours after its ingestion.
4. The absence of bile-staining of the vomitus or fluid obtained at lavage.
5. The presence and passing of meconium gradually showing more and more the appearance of bile.
6. The absence of any sign of digested milk in the stools as late as the seventh day.
7. The uniformly subnormal character of the temperature.
8. The persistent loss in weight.
9. The anuria.
10. The fact that the mother had hydramnios.

An important point in the diagnosis, first pointed out by Wyss—the absence of bacteria from the meconium—we did not observe.

The presence of hydramnios is of no little importance in making a diagnosis of this condition. Opitz observed that of 26 children born of mothers with hydramnios, but five were normal. It is remarkable, too, that of six cases of complete obstruction diagnosed during life and of which the reports of the autopsy findings were accompanied by complete clinical histories, in four, those of Porak and Bernheim (1891), Macé (1899), Wyss (1900), and Voron (1904), note was made of the presence of hydramnios on the part of the mother; while in two, those of Brindeau (1895) and Maygrier and Jeannin (1900), there was no statement as to its presence or absence. Under conditions such as were present in our own case, the fact that the fœtus could not swallow, or at any rate absorb, any great quantity of the liquor amnii, may account on the one hand for the unusually large amount of amniotic fluid present, and on the other for the emaciated condition of the child. As the most common congenital malformation of the digestive tract is undoubtedly stenosis of the pylorus, it appeared permissible to attribute the vomiting to such an abnormality—a supposition which was strengthened when it was noted that the vomiting did not occur with each feeding, but later when the stomach had been overloaded. Moreover, the passage of bile-stained meconium indicated that the gut was patent below the ampulla of Vater; and such being the case, the question to be decided then was, whether the obstruction was complete or partial. The absence of signs of milk in the stools was almost as significant as the absence of bacteria, while the anuria, hypothermy, and progressive loss of weight could only be explained by some serious interference with the body functions.

A laparotomy was performed under chloroform anæsthesia by Dr. W. F. M. Sowers, acting resident surgeon of the hospital, at noon, September 25, 1904. On opening the abdomen the stomach immediately came into view. The obstruction was not definitely located, and as it was thought best to avoid any unnecessary delay, the most accessible loop of ileum was secured and a typical gastro-enterostomy was done. The duration of the operation was about 25 minutes. The abdominal incision was closed with through and through sutures and the child was taken from the table in excellent condition. It came out of the anæsthetic well, and seemed much better. Salt solution was given per rectum, but was badly retained. The temperature began to rise during the afternoon and the child died at 2 a. m., September 26, 14 hours after the completion of the operation.

Apart from the case referred to above, reported by Maygrier and Jeannin, I have found no other in which gastro-enterostomy had been done on the new-born child. The operation has, of course, been successful in older children, where the stenosis has been incomplete, but Abel's favorable result in a child of 8 weeks, weighing over 4000 grams, is probably the most satisfactory one reported.

Péry has advised against operation in all cases of complete occlusion of the gut, as the results have invariably been fatal. On the other hand, without operation the prognosis is worse, for there is no possibility of recovery. Moreover, the bad results shown in the cases collected by Kuliga, Braun, Letoux, Savariaud, and Weill and Péhu have been in operations lower down in the intestinal tract where the distal portion of the gut had practically no lumen; and in many instances the difficulty of absolute accuracy of diagnosis delayed the operation until there was no possible hope for a favorable result.

Weill and Péhu insist that where the symptoms are not definite delay is permissible, but that the earlier the operation the greater are the chances of its being successful. This applies chiefly to cases where the obliteration of the gut is incomplete, for the early appearance of severe symptoms would, of course, point to a more complete occlusion and render the prognosis grave.

Autopsy.—At autopsy twelve hours after the death of the child there was found the following condition:

The body was that of a well-nourished male child 48 cm. in length. Rigor mortis was slight. The skin appeared normal except for some areas of discoloration. In the abdominal wall to the right of the linea alba there was a surgical incision about 7 cm. in length extending from the costal margin to a point about 1 cm. below the umbilicus.

On opening the abdomen and thorax the condition of complete situs transversus was observed.

The heart, of about normal size, lay almost entirely to the right of the mid-sternal line. The apex of the heart was 4 cm. from the mid-line in the 5th interspace. The foramen ovale and the ductus arteriosus were still patent, the heart otherwise was normal.

The lungs were of normal color and consistency both externally and on section. The right lung consisted of but a single lobe, showing, however, a small incisure opposite the sixth rib at its anterior border, indicating the probable line of division of the two lobes.

The left lung was made up of three lobes, which were fairly well defined. The lower and middle lobes were completely divided by a fissure; the upper and middle lobes, however, though separated completely on the posterior surface, were only indicated on the anterior surface by a notch just above the heart. The diaphragm reached the same height on both sides, due no doubt to the greatly distended stomach in the right hypochondrium.

The spleen was located in the right hypochondriac region in normal relation to the surrounding organs. The organ measured 2.75 x 1.25 x .5 cm., being of about normal size, consistency, and color.

The liver was of about normal size, measuring 7 x 3½ x 3 cm. and of reddish brown color. On the anterior surface of the right lobe was seen a hæmatoma measuring about 1 cm. across, which was produced by a slight injury at the operation. The organ had a large left and a small right lobe. The large left lobe occupied the greater part of the left hypochondrium. The gall bladder was observed lying on the inferior surface of this lobe about 1½ cm. from the mid-line and not extending quite out to the edge. The right lobe seemed rather larger in proportion than normal. Tracing out the bile duct, it was seen to have a normal course and was patent throughout.

The pancreas with its head in the left half of the epigastric region extended into the right hypochondriac region, so that its tail touched the mesial surface of the spleen. Projecting from the inferior edge of the pancreas to the right of the head were two small accessory pancreatic lobes, the longer measuring about 1½ cm. in length, and the shorter about ¾ cm.; their diameters were 4 and 2 mm., respectively. The larger of the lobes was directly continuous with the pancreas, while the smaller joined the larger close to its proximal end. These accessory portions extended out between the layers of the mesocolon. The duct of Wirsung was patent.

The kidneys were of about equal size, measuring 3.5 x 1.75 x 1.25 cm. The right kidney was placed slightly higher up in the body cavity than the left. On section the organ seemed normal.

The stomach was greatly dilated, measuring 7 x 4 x 3 cm., and occupied the greater portion of the epigastric and right hypochondriac regions and extending downward occupied a considerable portion of the umbilical and right lumbar regions. The stomach wall was everywhere smooth and tense. The fundus except for marked distension seemed about normal. The pyloric end, however, lay lower in the abdominal cavity than normal, and on dissection was seen to extend toward the left to a point slightly below the head of the pancreas; here it ended abruptly. On searching for a continuation into the duodenum, no connection could be found, but lying just behind and to the left of the head of the pancreas was seen the blind end of the duodenum, separated thus by an interval of perhaps a centimeter from the blind pylorus. No structure such as a fibrous strand or obliterated portion of the bowel could be found connecting the two blind ends. To exclude the possibility of such a structure, the two blind ends were carefully examined and in each case the serosa was intact over the entire surface, showing no point at which a small strand might have been pulled away. At the pylorus there was a small nodule which at the time was somewhat suggestive of being a possible point of former communication. It showed, however, in a set of serial sections a small lumen extending out into the nodule which did not open upon the surface, but ended blindly. This nodule was small and fibrous, slightly raised above the level of the surrounding surface, and its surface appeared perfectly smooth. It measured about 2 mm. across.

The general shape of the stomach was preserved, showing no structure that suggested a pyloric band of muscle. On palpation also no pyloric band could be made out, but it was noticed that the anterior wall was perceptibly thicker than the posterior. On the posterior surface near the margin of the greater curvature the ileum had been brought up and a gastro-enterostomy performed. The wound showed no inflammation about it and seemed to be healing.

The organs were hardened in situ in formalin, and on opening the stomach it was found to contain gas, fluid, and a small amount of dirty grey material. The rugæ were all obliterated.

As mentioned above and as seen in Fig. 1, the duodenum began in a somewhat enlarged, perfectly smooth blind sac, just to the left and slightly above and behind the head of the pancreas. Very close to the top of the sac the pancreatic and common bile ducts entered. The papilla of Vater was distinctly made out. Beginning at the side of the pancreas the duodenum extended downward for 6 cm., acquiring a mesentery just below the level of the pancreas and then curving slightly to the left continued as jejunum. The three divisions of the duodenum could not be made out nor the point at which the duodenum went over into the jejunum. The duodenum contained a small amount of turbid yellowish fluid. The small intestine in its first 10 or 15 cm. was of practically normal size, but beyond was empty and very much contracted. The ileo-

cecal valve was situated in the left iliac fossa. The appendix measured 2 cm. in length. The ascending colon thus was on the left side and the hepatic flexure in the left hypochondrium. The colon then crossed over to the opposite side, forming the splenic flexure in the right hypochondriac region and descending in the right side formed a large sigmoid flexure which extended beyond the mid-line; it entered the pelvis to the right of the mid-line.

The arteries and veins also showed a complete and exact situs transversus in every detail. The aorta came off from the right auricle, arched upward and to the right, and then extended down on the right side of the vertebral column. From the arch were given off a left innominate and a right carotid and subclavian. Joining the lower portion of the arch of the aorta was the ductus arteriosus, which still remained patent. The long renal and intercostal arteries were naturally on the

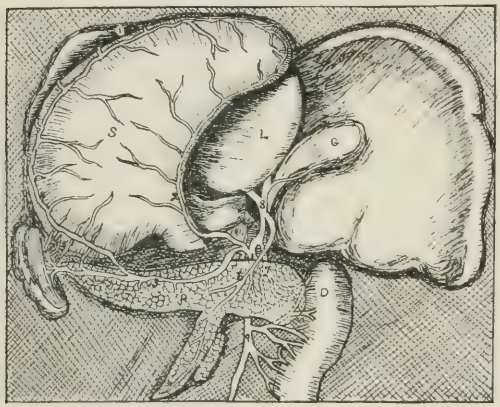


Fig. 1.

left side in this case. At the bifurcation of the abdominal aorta the left common iliac artery passed over the right and left common iliac veins to its position lateral to the latter. A scheme of the vessels has been diagrammatically shown in Fig. 2.

Unfortunately the arteries were not injected before section, and it was with some difficulty that the finer branches of the cœliac axis were traced out. As shown in Fig. 1, the general relation of the vessels could be made out. The cœliac axis divided into a right branch, which gave off the gastric and splenic arteries, and a left branch, the hepatic artery. The gastric artery passed rapidly to the lesser curvature along which it ran to the blind end of the stomach, where it anastomosed with the gastro-epiploica dextra, which ran along the greater curvature supplying branches to anterior and posterior surfaces, and at its end anastomosed, as stated above, with the gastric. From the splenic artery were given off several vasa brevia to the fundus of the stomach. The hepatic artery gave off its first branch to the head of the pancreas. Several of the small branches of this artery were followed down behind the pancreas, but were unfortunately lost before they could be traced to the end to see whether or not they supplied the duodenum. The next branch which came off from the hepatic was practically the key to the intestinal anomaly. At a point corresponding to the place at which normally the gastro-epiploica dextra (in this case sinistra) should have been given

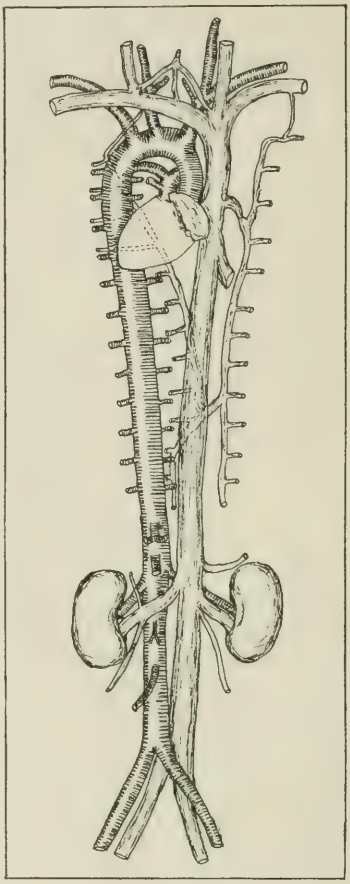


Fig. 2.

off, there was found a large artery which after giving off several small branches to the pancreas, sent the greater number of its branches to the accessory lobes of the pancreas, mentioned above. The pyloric branch of the hepatic artery was also absent. The hepatic artery, after giving off a small branch to the gall bladder, passed by two branches to the liver. As far as could be made out, the duodenum was supplied entirely by the superior-mesenteric artery.

The pulmonary artery came off from the left ventricle. It

gave off first the right pulmonary artery, which divided into two branches; next above, the ductus arteriosus; and lastly, the left pulmonary artery, which divided into three branches before entering the lung. In like manner there were three pulmonary veins on the left side and two on the right.

The vena cava superior was situated to the left of the vertebral column. The right innominate vein crossed in front of the right subclavian and carotid and the left innominate arteries to join the left innominate vein below the cartilage of the first rib, to form the vena cava superior, which was joined a short distance below by the vena azygos major. The inferior vena cava ascending on the same side emptied together with the descending vena cava into the left auricle. The vena azygos major drained the entire left intercostal region and anastomosed below with the ascending lumbar and above with the subclavian vein. The vena azygos minor superior drained

The pancreas was practically normal, except for one portion of the smaller accessory lobe, which consisted almost entirely of fibrous tissue with a few islands of epithelium scattered through it. The connective tissue was *particularly cellular* about these remaining alveoli, but showed no small celled infiltration.

The kidney, except for some uric acid infarcts, was normal.

The duodenum was practically normal.

The anterior wall of the stomach on section was seen to be thicker than the posterior, due to a difference in the size of the muscle layer, which was considerably thinner over the posterior wall. A section through the nodule at the pyloric end of the stomach showed a lumen in communication with that of the stomach. When traced through the serial sections the lumen was seen to bend over near the top of the nodule and to extend parallel with the stomach wall for a fraction of a milli-

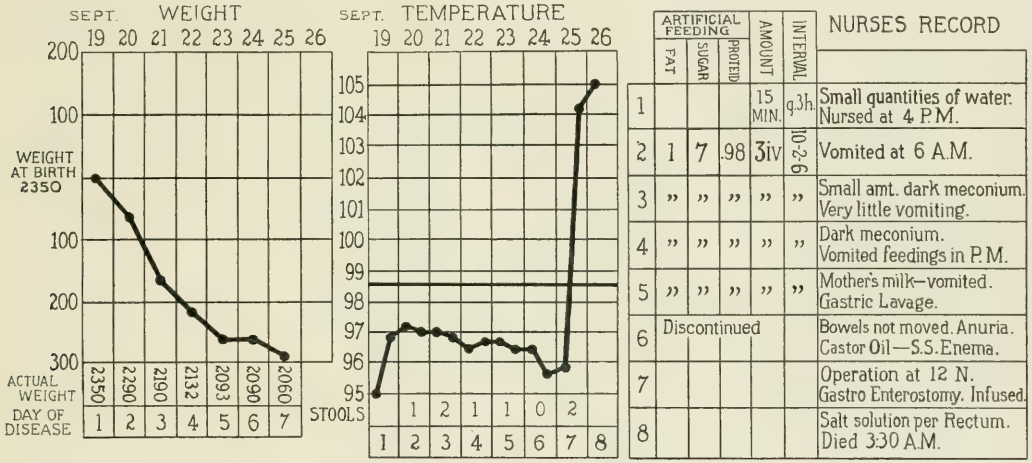


FIG. 3.

the 5th to 9th right, and the vena azygos minor inferior the 10th to 12th right intercostal spaces. These two veins joined and emptied into the major in the 9th left interspace. The right superior intercostal drained the upper four spaces and anastomosed with the vena azygos minor superior. The left draining the upper three was received into the major. The left suprarenal emptied into the vena cava, the right into the renal vein. The left spermatic vein joined the vena cava at the angle formed by it and the entering renal vein. The right joined the renal vein on that side.

Microscopical Examination.—The heart, lungs, and spleen were practically normal.

The liver cells showed considerable fatty change, and in some rather sharply defined areas the cells were filled with brownish black pigment. There was a slight increase in fibrous tissue about the portal spaces, and also focally throughout the section small areas of fibrous tissue were seen.

meter and then it gradually narrowed down and finally ended blindly. The lumen was lined by high columnar epithelial cells, with large vesicular nuclei lying at the very base of the cells which greatly resembled duct epithelium. Between the normal stomach epithelium and these cells there was an abrupt transition. The submucosa was made up of cellular fibrous tissue and in its outer portion ran small bundles of smooth muscle. On one side of the nodule the muscle layers of the stomach ended abruptly in a slight thickening, but on the other side the bundles grew gradually thinner and shaded off into the small bands of muscle that ran along the outer border of the nodule. Just to one side of the nodule there was just under the muscularis mucosæ a large island of gastric glands cut transversely. On tracing it through the series it spread out into the general lining of the stomach, and so represented merely a fold in the mucosa. The serous surface was everywhere intact and showed in that portion of the section near the

gastro-enterostomy wound a slight exudate of leucocytes and red cells.

Upon examination of the available literature it was found that as early as 1752 James Calder reported a case of atresia of the duodenum. The case in brief was as follows: "At section the stomach was found in good condition. The pylorus felt hard as though it contained something; on opening, a gland-like piece of tissue was found closely adherent to the wall all around, with no perforation anywhere. Below this the duodenum was double to about 1 inch above the jejunum." The next case was reported by Daniel in 1765, in which there was absence of heart, lungs, liver, pancreas, spleen, and left kidney. Beginning with the nineteenth century, cases were reported with greater frequency; but as practically all the cases of duodenal atresia up to 1901 were collected by Cordes, it has been thought best to tabulate only those cases in which atresia of the duodenum was present above the papilla of Vater.

Case No.	Reported by	Age.	Symptoms.	Location of Atresia.	Stomach content.	Intestinal content.	Liver and Pancreas.	Other Malformations.	Etiology.
1	J. Calder. Med. Essays, Edin., vol. I, p. 167. 1752.	0	0	Pyloric end of duodenum	0	0	0	0	New growth?
2	Daniel. Med. Gutachten, Leipzig, 1776, p. 276. 1765.	Miscarriage	0	Close to stomach.	0	0	Both absent.	Heart, lungs, spleen, left kidney absent.	0
3	Aubrey. Med. Chir. Ztg., Salzburg, IV, p. 269. 1808.	6 days.	Vomiting.	Above papilla.	0	0	0	Pancreatic duct absent. Bile duct ended in pancreas.	0
4	Crosby, Leonard. Asso. Med. Jr., No. 197. 1856.	4 days.	Vomiting. Small stool.	Above opening of common duct.	Brownish fluid and blood clot.	Meconium.	Normal.	0	0
5	Wilks. Trans. Path. Soc., London, XII, p. 102. 1861.	38 hrs.	Vomiting meconium at intervals.	Immediately above Papilla of Vater.	Greenish fluid.	Meconium.	Normal.	0	0
6	Hirschsprung. Schmidt's Jahrbuch, 117, S. 310. 1861.	5 days.	Vomiting (like meconium.) Meconium stool	Above papilla.	Dark green semi-fluid material.	0	Liver normal Pancreas 0.	0	0
7	Hervey. Bull. Soc. Anat., Paris, XLV, p. 338. 1870.	5 days.	Vomiting (coffee-ground). No stool.	Above papilla.	Thick black material and milk curd.	Meconium.	0	0	0
8	Hempel. Jahrb. f. Kinderheilkunde, VI, p. 381. 1873.	5 days 20 hrs.	Vomiting. Scant stool.	Middle of vertical portion.	Pale, grey, opalescent fluid.	Meconium mushy green	Liver normal Pancreas 0.	0	0
9	Theremin. Deutsch. Zeitschrift f. Chir., VIII, p. 34. 1877.	4 days.	Icterus. Vomiting. Meconium stools.	Above papilla.	Coag. milk. mucus.	Meconium.	0	0	0 0
10	Silberman. Jahrb. f. Kinderheilkunde, X, p. 385, 1882.	4 days.	Vomiting, yellow. Meconium stools.	Above papilla.	Milk.	Bile stained mucus.	Liver enlarged. Pancreas normal.	0	
11	Emerson. Archives of Pediatrics, Philadelphia, VII, p. 684. 1890.	4 days 10 hrs.	Vomiting, dark-brown, greenish, watery fluid.	Just above papilla.	Dark grumous fluid.	Empty.	0	0	0
12	Northrup. Archives of Pediatrics, Philadelphia, VII, p. 684. 1890.	0	0	Just above papilla.	Little mucus or meconium	Bile-stained mucus.	0	0	0
13	Rosenkranz. Inaug. Dissert. Med. Facult., Königsberg, Preussen. 1890.	4 days.	Icterus. Vomiting breast milk. Meconium stools.	Above papilla	Semi-fluid.	Almost empty.	0	0	0
14	Porak and Bernheim. Bull. Soc. Anat. de Paris, LXVI, p. 230. 1891.	5 days.	Vomiting black material. Passed no meconium.	Above papilla.	0	Meconium.	0	0	0
15	Hobson. Brit. Med. Jour., p. 639. 1893.	3 days.	Vomiting mucus.	Above papilla.	Ruptured into peritoneal cavity.	0	0	0	0
16	Collum. Tr. Soc., Path. Lond., XLVI, p. 60. 1894.	6 days.	Vomiting milk. Meconium per rectum.	Above papilla.	0	Meconium.	0	0	0
17	Markwald. Münch. Med. Wochenschr., No. 14, p. 265. 1894.	4 days.	Vomiting.	Above papilla.	Small amount of glairy mucus.	Meconium.	Irregular lobulation of liver.	Atresia œsophagus and rectum.	Inflammation of mucosa of stomach and duodenum.

Case No.	Reported by	Age.	Symptoms.	Location of Atresia.	Stomach content.	Intestinal content.	Liver and Pancreas.	Other Malformations.	Etiology.
18	Champneys. Brit. Med. Jr., Mar. 20, p. 718. 1897.	5 days.	Jaundice. Vomiting watery yellow fluid.	Just above papilla.	0	Meconium.	0	0	0
19	Mace. Bull. de Soc. Obst. de Paris, 1899, p. 2. 1899.	3 days.	Vomiting fluid.	Above papilla.	0	0	0	0	0
20	Wyss. Brun's Beiträge zur Klin. Chir., p. 631. 1900.	6 days.	Vomiting of meconium. Small amount meconium per rectum.	Between upper and middle portion. Above papilla.	Meconium, black material and gas.	Meconium.	Liver large and bright red. Pancreas normal.	Vascular. Club-foot.	Absence of pancreaticoduodenal artery.
21	Wyss. Brun's Beiträge zur Klin. Chir. p. 631. 1900.	1¼ days.	Vomiting blood a few times.	Above papilla.	0	0	0	Hydrorrachis.	0
22	Sick. Münch. Med. Wochenschrift, 47, I, p. 170. 1900.	0	Vomiting.	Above papilla.	0	Meconium.	0	0	0
23	Maygrier and Jeannin. Bull. de Soc. Obst. de Paris, III, 112. 1900.	5 days.	Vomiting of all nourishment. No stools.	Above papilla.	0	Meconium.	0	0	0
24	L. Cordes. Archives of Pediatrics, Vol. 18, p. 401. 1901.	4 days.	Vomiting yellow fluid and nourishment.	Just above papilla.	None.	Meconium.	Normal.	0	Developmental error.
25	Katz. Bull. et Mém. Soc. de Paris, LXXVI, p. 471. 1901.	6 days.	Vomiting brown material.	Near pylorus.	Brown viscid fluid.	Meconium.	0	0	0
26	Voron. Lyon Médicale, CII, p. 727-736. 1904.	5 days.	Vomiting milk. No bile. Passed meconium.	Above papilla.	0	Meconium.	0	0	0
27	Little and Helmholz.	7 days.	Vomiting amniotic fluid right after birth, and later nourishment. Meconium passed with increasing amount of bile.	Absence of pylorus and duodenum as far as papilla.	Gas and small amount of greyish mucus.	Bright yellow semi-fluid meconium.	Liver fatty and focal sclerosis. Pancreas accessory lobes.	Situs transversus. Vascular.	Absence of superior pancreaticoduodenal artery of pyloric, and of gastroepiploica sinistra.

In all the cases which have here been tabulated, with one exception, that of Calder in 1752, the atresia was some distance below the pylorus, and as a result of the constriction being so placed there was not only a greatly dilated stomach but also a distended proximal portion of the duodenum, as large or larger than the stomach. Between these two large sacs there was a constriction due to the pyloric band of muscle, which gave the typical hour glass appearance. Further, in no case was there a complete absence of a portion of the bowel, but merely an obliteration of the lumen for a longer or shorter distance. Lastly, all the cases had in common some structure connecting the proximal and distal portions of the duodenum. In a number of instances in which the connection was described as a strand of fibrous tissue, Wyss believes that microscopic examination might have revealed a small lumen lined by epithelium, thus representing a very much constricted and atrophic portion of the bowel.

The present case differed quite markedly from the rest: 1. There was but a single large sac, proximal to the atresia. 2. There was an involvement of both the duodenum and pyloric end of stomach. Not only was there an absolute absence of connection between the proximal and distal portions of the bowels, but also a complete disappearance of the pylorus and of the duodenum as far as the papilla of Vater.

To explain atresia occurring along the intestinal canal a great number of theories have been advanced. As early as 1839 v. Ammon put forward the theory that this condition was due to an error in development, being an arrest of development at a period when the alimentary canal still consisted of two parts. Since the great advances in embryology this theory in its completeness can no longer be held, though error in development of a different nature may still in an indefinite way be held responsible for this malformation. In 1858, Streubel, and somewhat later Valenta, sought to explain atresia by volvulus, especially when the loop of intestines was filled with meconium, which prevented its return to the normal position. This secondarily set up a peritonitis. Then in the eighties Schottelius and Silberman suggested a primary peritonitis most probably of luetic nature, as the most satisfactory causal agent in this condition. Abnormally long persistence of the omphalomesenteric duct, traction due to hernia, and embolism of the superior mesenteric artery, have been

advanced in individual cases to explain atresia. Lastly, circulatory disturbances, both changes in the arteries due to disease (Küttner) and congenital absence of arterial branches (Wyss) were suggested. In one of the cases reported by Wyss the absence of an arterial branch explained the condition.

This last idea seems to offer the most plausible explanation for the conditions found in the present case. The pancreaticoduodenalis superior, the gastro-epiploica sinistra, and the pyloric branch of the hepatic artery are absent, and the gastrica and gastro-epiploica dextra anastomose with one another over the blind end of the stomach. Apparently as a result of this lack of blood supply there has been a complete disappearance of the pyloric portion of the stomach and of the duodenum as far as the papilla of Vater, although at some time in embryonic life the continuity between stomach and duodenum must have existed.

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A CASE OF CONGENITAL URETHRAL STRICTURE ASSOCIATED WITH HEMATURIA AND SYMPTOMS SUGGESTING RENAL DISEASE.

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Congenital stricture of the urethra, though a condition by no means unrecognized, is sufficiently rare to be always of interest. The cases, moreover, presenting urethral stricture in which a *positive* diagnosis of its congenital nature can be made must always be only a small proportion of those cases in which such a diagnosis seems *probable;* for, with a urethral stricture in a patient past puberty (or indeed even in younger patients) we must have also a perfectly negative urine examination before post-inflammatory or post-traumatic stricture can be excluded. And it is notorious how rare perfectly normal urines are, particularly in the out-patient departments where these cases are usually studied. If the urine shows signs of a previous urethritis, that urethritis cannot be excluded as the cause of the stricture; and, though there might be other reasons for considering its congenital nature probable, such a diagnosis, with shreds in the urine, could never be positive. For these and other reasons the condition, though usually recognized in the text-books, is almost always said to be a rare one. "Extremely rare," White and Martin call it; Treves, in his discussion of urethral stricture, does not mention it; Walsham admits that "a few cases are congenital;" and Sir Henry Thompson, in his clinical lectures, says nothing about it. If the whole subject has received such scant consideration, it is obvious that any associated clinical features have been either unobserved or unrecorded.

The patient here reported was a white boy 13 years old, who came to the genito-urinary clinic of the Johns Hopkins Hospital during the winter of 1904-1905. His complaint was pain in the left side after urination and the passage of blood clots with the urine. He had one brother living with tuberculous disease of the hip, but his family record was otherwise a good one. His own previous history was negative. Bronchitis and mumps were the only acute illnesses from which he had suffered, and previous genito-urinary trouble (either venereal or otherwise) was emphatically denied. Though his previous health had been good, his disposition had never been energetic and he had complained to his mother frequently of "feeling tired." The onset of the present illness occurred suddenly four days before admission, up to which time he had had no urinary symptoms. It was attributed by the patient to severe muscular strain (lifting a heavy weight in the store in which he worked), and the first symptom was a sudden uncontrollable desire to micturate. This was followed, when urination occurred, by severe urethral burning and the urine passed was seen to contain clots of blood. Pain in the left side, about over the ureter, was present during the passage of the clots, and also subsequently. It was of a stabbing character. These attacks were repeated practically every time the patient passed his water during the next four days. At times blood was absent and then the pain was less. At other times hematuria was marked.

On admission the examination of the patient was almost negative. His general physical condition was good and his genitalia normal except for a small meatus about the size of a pin-head. There was slight tenderness on pressure over the bladder and particularly over the course of the left

ureter. The urine was cloudy, containing epithelial cells and leucocytes, but neither red blood corpuscles nor organisms. It was acid in reaction, but examination for tubercle bacilli was negative. A meatotomy was done to make subsequent urethral exploration possible and the case was thought to be probably one of disease (tuberculous or calculous) of the left ureter or kidney. As no blood could be found in the urine at this examination, it was thought that the patient had probably mistaken high coloration for hemorrhage. An X-ray photograph was taken of the left side and proved negative, as did also a second examination of the urine for tubercle bacilli. On the second and third visits the urine was again negative for blood, though the patient claimed that, at home, he still occasionally passed some, and that some pain was still present along the ureter. On the fourth visit the patient was suddenly taken in the dispensary with an attack of nausea and vomiting, accompanied by pain over the bladder and left ureter, and by the passage of clouded, bloody urine. This attack was, he said, similar to those he had been having. A cystoscopy was immediately attempted in order, if possible, to determine the source of the hemorrhage, but it was impossible to insert the instrument more than ½ inch into the urethra beyond the meatus. A small No. 10 F. rubber catheter could be passed into the bladder with difficulty. The patient was sent into the hospital to allow him to recuperate from his attack and to have him given tuberculin. During the first two days of his stay in the hospital he had some pain in the sides and some hematuria. On the third day his urethra was again examined with instruments and it was found that there were two points of distinct narrowing—one about ½ inch behind the meatus and running ¾ inch. back along the urethra, the other in the bulbo-membranous urethra. A filiform and No. 8 F. follower were passed with some difficulty; and all instrumentation caused severe burning pain when the tip of the instrument reached and was passing through the prostatic urethra, in spite of anæsthetization with 4 per cent cocain. A diagnosis of stricture (probably congenital) was made, the patient was put on urotropin and dilation advised. The urine at this time contained large numbers of leucocytes, a few epithelial cells, a few red blood corpuscles, but no organisms. The patient was complaining of some frequency of micturition at night and examination by hydraulic distension showed a moderately contracted bladder. Gradual dilation with sounds was then instituted, instruments being passed every day, always with cocain anæsthetization, without which they could not be borne, and even with which severe burning pain was always noticed when the sound passed through the prostatic urethra. The symptoms disappeared almost as soon as sounding was started and they did not reappear. Three features of the urethral narrowings were noticed during the sounding which were different from the more usual characters of inflammatory stricture. In the first place, progress in dilation was extremely slow; in the second place, examination of the urethra with a bulbous bougie showed a narrowing of the lumen extending along the urethra for about ½ inch at the sites of both "strictures" with an unroughened urethra between—rather than a localized cicatrix (causing a definite "catch" on the acorn of the bougie) with definite secondary roughenings along the urethra characteristic of inflammatory stricture; and thirdly, the spasmodic character of the posterior stricture was quite marked, the instrument always being difficult to insert until pressure had been exerted for a while and always causing a burning pain. The patient was kept in the hospital for four weeks, but no good tuberculin being obtainable the test was not applied. Dilation was, however, kept up (every day for two weeks, then thrice weekly) and urotropin administered internally. On discharge symptoms were still absent and the urethra could accommodate a No. 16 F. sound. The urine was clearing but still contained a few pus and epithelial cells. Two months later dilation had progressed until a No. 20 sound could be passed. The boy was still perfectly free from symptoms. On account of the expense urotropin had to be abandoned and methylene blue was substituted for it. The day after its adoption the boy showed, immediately following his instrumentation, typical symptoms of cocain poisoning, except that the pulse remained slow and good. The usual amount and strength of cocain had been used, but the patient had failed to void after instrumentation. He became irrational, complained of great weakness and nausea, and sweated profusely. He was immediately catheterized and then given atropine and morphine subcutaneously. Nausea and weakness persisted, and as the patient complained much of a bad taste in his mouth with eructation his stomach was washed out. It was found to contain a strong solution of methylene blue. After lavage with large amounts of water the symptoms improved, the bad taste disappeared, and the patient soon recovered entirely. One week later the urethra could accommodate a No. 22 F. sound and symptoms were entirely absent. The urine was perfectly clear, contained neither shreds nor cloud, was alkaline in reaction, contained no albumen, and was negative microscopically. A stained centrifugalized specimen from the third glass showed some meatal organisms lying in squamous epithelial cells, but there was no sign of bladder infection. Cystoscopy was attempted, but the cystoscope (No. 24 F.), though it passed the anterior urethra easily, caught in the prostatic portion where the contact of its tip occasioned severe burning pain.

It is not at first sight easy to offer in this case a satisfactory pathological explanation for the symptoms. Hemorrhage is, of course, a not infrequent accompaniment of inflammatory urethral stricture, and it is clear enough how, in these cases, granulation or other features of an inflammation might be the source of blood in the urine. If the stricture is, however, a congenital one, there seems to be no good pathological reason why hematuria should be a clinical feature. Mere narrowing of the urethral lumen without the presence of granulations or other features of inflammation would not, it would seem, account for bloody urine. It seems probable,

however, that the blood in this case came from the verumontanum. Hemorrhage in chronic urethritis not infrequently makes its appearance late in the course of the disease, and the blood is passed by such patients in the last act of micturition when the prostatic urethra is vigorously compressed. Moreover, topical applications of silver nitrate and other caustics—made by means of an instillator which reaches into the prostatic urethra—quite often stop the hemorrhage. So that bleeding from the verumontanum in inflammatory conditions of the prostatic urethra does occur. It is also seen as an independent condition without the association of inflammation as a cause. During the winter of 1903-1904 I saw in the practice of Dr. Young a patient who was brought to him for hematuria without cause or accompanying symptoms. The boy—13 years of age—had been passing blood for some time, but he had no pain or other trouble suggesting kidneys or ureter as the source of the blood. He denied venereal infection and the absence of shreds in the urine corroborated this denial. Cystoscopy showed a normal bladder and the urine from both ureters was clear. When the cystoscope was pulled well out so that its window commanded the prostatic urethra a large, swollen, and hemorrhagic verumontanum could be seen. This was evidently the source of the hemorrhage.

There is, then, abundant clinical evidence to show that bleeding may occur from the verumontanum, and it is noteworthy that in this patient *every time the sound passed over the verumontanum there was severe stinging and burning pain.* In other words, just those clinical features were present which we should expect if the colliculus seminalis were enlarged and inflamed. Such an enlargement *does* occur and is one of the forms of congenital stricture described in the literature. Ziegler, in his account of the genital malformations seen at birth in the male, says: "An abnormal narrowness may exist in a portion of its (the urethra's) course or throughout its whole extent. *Its lumen may be compromised by an hypertrophy of the colliculus seminalis.*" There is then good ground for assuming that the hemorrhage in this case came from an enlarged verumontanum.

The interesting features presented by the case reported may be summarized as follows:

1. This patient presented a urethral stricture in which a positive diagnosis of its congenital nature could be made. Such a diagnosis was warranted by: (a) The history, from which all record of urethral traumatism or of venereal infection was absent. (b) The association of an obvious congenital stricture at the meatus. (c) The complete cure of the clinical manifestations by proper treatment of the stricture. (d) The presence of clear urine and the absence of symptoms after the actual stricture had been dilated.

2. The second point of interest was offered by the clinical symptoms presented. These were nausea and vomiting, hematuria, and pain over the left ureter. They suggested renal or urethral disease, and obscured the diagnosis which was really only cleared up by the therapeutic test.

3. In the third place, this case suggests that another item must be added to our already long list of causes for hematuria, and that congenital stricture may be associated with blood in the urine, the source of which may probably be an hypertrophied verumontanum.

SYNESTHESIA.[1]

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The subject of synesthesia, for many years, has attracted a good deal of attention in Germany, France, England, and Italy, and latterly a number of cases have been reported in America. The phenomena of this interesting condition are known as "secondary sensations," or "associated sensations," by which are meant constant and involuntary subjective impressions associated with actual perceptions. Synesthesias are found in many persons to a limited degree, but cases showing numerous and well-marked features are exceptional and always of interest.

Not a few individuals experience a shivering sensation at the squeak of a pencil as it is drawn over a slate, or at the sound produced by the tearing of a piece of linen. Others have their teeth put on edge when the filing of a saw is heard. Such sensations are spoken of as *sound feeling.*

Color hearing or *sound seeing,* as it is sometimes called, is among the rarer types of associated sensations. It is the constant and involuntary visualization of color associated with some definite sound. Goethe and Hoffman were among the early observers who referred to the existence in certain people of this peculiar faculty. Sachs in 1812 published an account of the phenomena as possessed by himself and his sister. Nussbaumer first excited general interest in the subject by a description of his own case before one of the scientific societies in Vienna. An eminent neurologist, who was present, considered his sensations as pathologic and predicted some oncoming mental disturbance. Nussbaumer, however, remained well. In 1881 Bleuler and Lehmann, the former of whom had the idiosyncracy, reported the result of their inquiries among 596 normal individuals. They found that 12.8% of these were more or less synesthetic. Among other observers may be mentioned Galton and Fechner, and, in America, Baldwin and Miss Calkins. Flournoy's book "Des

[1] Read before the Johns Hopkins Hospital Medical Society, February 6, 1905.

Phenomènes de Synopsie," contains a most exhaustive study of the subject.

Color sensations remain constant in the same person but vary in different individuals. For example, the sound of the vowel *a* is red to one, blue to another and black to a third. Colman has shown conclusively that the colored alphabet used in teaching children their letters has nothing to do with color audition. In one family all of the members were synesthetic, and had learned their letters out of the same book but possessed nothing in common in their color associations. The deeper vowel tones usually suggest the shades, and the higher vowel tones the tints of colors.

Again, the kind of sound giving rise to color sensations varies for different individuals. In one case color sensations are produced by the vowel sounds, in another by the tones of a speaker's voice, while many associate musical tones, the days, numbers, months, seasons, odors, taste, and touch with corresponding colorations. Some people when reading rapidly, can detect misspelled words by the wrong color impressions received.

When light instead of color is associated with sound we have what is known as photism; when a color, or some definite image, suggests a sound we have phonism. Cases of singers have been cited who could pitch their voices accurately when they thought of the corresponding tint or shade of color, and certain violinists have been known to tune their instruments by employing a similar method. Galton reports the case of an individual who could read the colors of a gaily decorated wall-paper as syllables and sounds.

Color hearing may prove annoying and confusing. The inevitable color sensations associated with tones destroy in the minds of some subjects the strains of music, and the incessant play of colors seen while reading or writing is most irritating to others.

Another interesting but more common type of synesthesia is known as the *number-form*. It is characterized by the visualization of serial numbers, dates, important events, etc., as occupying definite geometric positions in space. Such a condition opens up a wide range for the formation of mental diagrams or symbols, which are so far-reaching that to the average mind they are as inconceivable as is space itself. They are usually circular, spiral, or wave-like in shape and are peculiar to the impressions of the possessor. They serve as ready reminders of past occurrences and are generally helpful in mental calculation and memorization, but for higher mathematics and abstract speculation they are, in the main, a hindrance.

As to the true nature of synesthesias, nothing positive is known. Neiglicki and Steinbrügge regard the phenomena as pathologic; on the other hand, Chabalier, Urbantschitch, and Baldwin consider them to be strictly physiologic. Ziehen says that synesthesias are more common among the sane than among the insane. Baldwin states that "synesthesias of all sorts cannot be considered specifically abnormal, certainly not morbid, but belong to the realm of the unusual and idiosyncratic, within which explanation is difficult"; he adds that, "although subjective, they are not hallucinations."

Heredity is a proven factor since the condition has been observed in two or more generations of the same family. Males appear to be more frequently affected than females, yet in the latter the color visualization is the more intense. The photisms, color-hearing, and phonisms of early life are more vivid and last longer than those acquired during adolescence, and all tend to grow less distinct with advancing years. The number-form seems to exist throughout life unchanged.

History of Cases.

The synesthetic family to which I shall refer more especially includes the father and all of his children—three daughters and two sons.

Case 1. Mr. G., a clergyman, aged 49 years, is a man of high attainments but of a retiring disposition. He states that since his early childhood he has associated the sound of each letter of the alphabet with a definite color value. The letters *f, j, k, r,* and *x* are a reddish-brown; *o* and *c* are snow-white; *a, d, g, n, s, q,* and *u* have the appearance of glycerin. The remaining letters are of a dull lead color, shading down to black. When a little boy he was laughed at by his older brothers and sisters because he "anxiously asked them" why a certain bay horse was given "the white name of Charlie."

Words receive their color almost entirely from capital letters. He does not know of a similar affection in any of his antecedents, but his niece, a sister's daughter, has the color audition form of synesthesia, and also the involvement of the pain sense. A vivid purple, she says, is seen when she is suffering intense pain.

Mr. G. has never mentioned his associated color sensations to his niece or his children, which goes far to prove that he is unduly sensitive about his idiosyncracy.

Case 2. Miss A., aged 23 years, is the oldest daughter. She is a clever young woman, a teacher in one of the large female institutions of the South, and, incidentally, is fond of matters psychologic. She, and, indeed, all of her brothers and sisters seem to have inherited their father's quiet and rather shrinking nature. My attention was first directed to the study of synesthesia by her somewhat startling questions: "Why are the keys of the piano colored in my mind?" and, "Why is it I sing or play anything familiar by color?"

Before she learned the alphabet she refused to call her mother "mother" because the name looked ugly to her; she preferred "mamma" on account of the more cheerful and pleasant color association.

The letters of the alphabet assume no definite form but come out on a light background as they are spoken; some of them are transparent, most of them are opaque, all are colored.

Words, whether thought of, heard, or written, get their color, as a rule, from the prominent initial letter sound. "Gray words" are due to the "g" sound, as *gray, grief, get,* etc. "Yellow words" have a prominent "s" or "*y*" *sound,* as *sweet, Xerxes, yonder,* etc. "Blue words" have the "l" sound, as *love, law, light,* etc. "Sunlight words" have the

"c" sound, as *child, chair,* etc. When she wishes to recall a name, tune, or any event, she first thinks of the associated color. The names of the seasons, months, and numerals, in fact all names, possess their characteristic coloring in her kaleidoscopic brain.

The higher musical tones are light in color, the deeper tones are dark, and the deepest are black. Some tunes are disliked because of unpleasant color associations. Melodies learned in her childhood retain the most vivid color effect, in fact, in all of my cases the earliest color impressions are the most distinct. The *tactile,* the *temperature,* and the *pain sense* are all involved but the stereognostic sense is normal. Hard objects when touched are dark in color; soft objects are light. If she feels something hot a dark gray is seen, if a piece of ice is grasped, white is promptly visible. A dull pain is of a dark lead color, a sharp pain is of a light steel color.

Case 3. Miss M., aged 22 years, is the most practical of the three sisters. She has an excellent memory for details and dates in general. She tells me that she has often lost her temper with her sisters because their color impressions were entirely discordant with her own. *Words* are colored by each letter which retains its individual color index.

She possesses to a marked degree the number-form of synesthesia. The numerals, whether counted in English, Greek, Latin, French, or Japanese, occupy the same fixed positions in space. She likes numbers as a general rule, particularly 3 or its multiples. The months of the year group themselves in a circular fashion and are comparable to the hour-marks on a clock dial. The hour-mark 5 is in the middle of January, 4 in the middle of February, etc. The alphabet, the list of the kings of England, the multiplication table, the catechism, and any series of important dates has each its specific mental diagram. These diagrams she and her younger sister call "roads," and once clearly visualized, they do not tend to fade, but serve as a ready means for memorization and recollection.

Tunes are not colored, but the keys of the piano are, and possess more or less human characteristics.

When an object is put into her hand she at once obtains a true mental image of its *form;* then follows an associated *color sensation.* For example, when a nickel was put into her hand, her eyes being shut, she said, "I feel a coin about the size of a nickel, but it is of a dark brown color." This phenomenon, as I take it, shows involvement of the *stereognostic sense.* The *pain sense,* the *temperature sense,* and the *tactile sense* are all slightly involved in her case as well as in that of her younger sister.

Case 4. Miss L., aged 20 years, has many accomplishments. She is clever with her brush, writes music, poems and short stories of more than usual merit. She has color hearing and the number-form both developed to a remarkable degree, and as noted in the cases of her older sisters, numbers, letters, and all words are associated with colors. The coloration of her words is due to the overlapping of the colors of the component letters. Capitals are more highly tinted or deeply shaded than are the corresponding small letters. In her case the consonants take on brighter hues than the vowels—the reverse being usually the rule. During early childhood she formed likes and dislikes for certain letters and numbers. "S" is a jolly, companionable letter; "d" is gloomy and unfriendly. Kindly letters are yellow and red, those "not fancied" are blue and purple.

The keys of the piano are colored, the high tones are light, the medium tones are dark, and the lowest are black. The key of F is green; that of G is yellow, and of C is blue. It is interesting to note that the colors of these musical letters do not agree with the coloring of the corresponding letters of her alphabet. She writes me that the G and D chords always make war upon the C chords, which are protected by the F chords. The figure 5 is a pleasant one. The figure 6 has always been disliked.

Numbers, serial events, poems, etc., that have been committed to memory, have, as in the case of her older sister, their characteristic "roads." These roads are usually seen in "rooms" which are bounded by points of the compass. The inherent tendency to arrange the points of the compass around her mental images—with a good deal of originality—she terms her *direction sense,* and she refers to it as one of the earliest dictates of her consciousness. The relation of the points of the compass varies but is constant for the associated concept. This is well shown in her mental diagrams for the "direction sense" of all the books she has read. When she thinks of the human body, certain books, sewing, painting, etc., she imagines herself as facing the southwest, but when embroidering and other acts are thought of she must face in the opposite direction. Curiously enough, the Hymnal and the Prayer-Book face from opposite directions, though she has been accustomed to see them bound together. When thinking of the months she sees a clock-dial diagram that of course is peculiar to herself.

Case 5. E., a youth of 17 years of age, is of less interest. The coloration of his alphabet is not vivid, and his *word coloring* is distinctly independent of the colors of the individual letters. Numbers are not colored, and the number-form of synesthesia is wanting. This boy is very intelligent and stands first in all of his classes.

Case 6. Master F., 14 years old, is an unusually clear-headed and logical youth. He has a goodly store of grotesque mental diagrams, which greatly aid him in his mathematical work and in recollecting facts. His clock-dial diagram is elaborate and embraces the seasons, the months, and indistinctly, the days of the months and of the week. He has no color sensations associated with sounds.

Summary.

The sensitive nature of Case 1 and his children reminds us of the advice given by Galton, viz., that synesthetic children should not be punished by teachers or teased by their playmates when they refer in all sincerity to their associated

sensations. Case 2 presents color audition, photisms, phonisms and involvement of the temperature, tactile and pain senses. Case 3 has a combination of color audition and the number-form of synesthesia and the involvement of the stereognostic sense. Case 4 is notable for the association of human characteristics with certain numbers, colors, and musical tones, and for the very odd mental diagrams. Cases 5 and 6 show fewer variations. The senses of smell and taste are not involved in any of the cases. Among other points worthy of note are the following: the direct transmission of synesthesia from the father to all of his children; that the color sensations are dissimilar, and those formed in early youth are more intense than those acquired later in life, and, that all tend to fade in time. On the other hand, the mental diagrams of the number-form remain unaltered, and serve as strongholds wherein past impressions are arranged in an orderly way and can be passed in review at will. Finally, all of our cases are, from an intellectual standpoint, far above the average; and are sane, healthy, and happy.

In conclusion, I desire to say that though the literature on synesthesia is abundant, relatively few contributions have come from general medical men. I believe that more careful study on their part would add something to the psychologic data and would not be void of practical results.

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CORRESPONDENCE.

KNOWLEDGE OF GREEK AND CORRUPTION OF LANGUAGE.

New York, April 7, 1905.

Editor Johns Hopkins Hospital Bulletin:

Sir:—The following remarks may be of historical interest and very timely at the present state of our disgraceful appendicitis, oophorectomy, gastro-saccharorrhœa onomatology:

Two men, the great physician, philologist, and noble patriot, Adamantios Koraïs, and a German physician, L. A. Kraus, almost simultaneously—about eighty years ago—made some remarks, the one on corruption of language, the other on the necessity to a physican to know Greek, which may be of interest at this present time.

Koraïs wrote: Νομίζω ὅτι ἡ διαφθορὰ τῆς γλώσσης εἶναι συγγενὴς νόσος τῆς διαφθορᾶς τῶν ἠθῶν καὶ κατὰ τοὺς ἱπποκρατικοὺς κανόνας ζητεῖ καὶ συγγενῆ καὶ παρομοίαν θεραπείαν.

(I consider that the corruption of language is a disease closely allied to corruption of manners, and demands also, according to Hippocratic canons, a similar course of curative treatment.)

L. A. Kraus: Pfuscher kannst Du ohne Griechisch werden, aber glaube mir, nie ein sicherer Arzt. Wer nur einigermassen die Erfordernisse zu einem Arzte, welcher mehr als jeder andere Mensch alle Lebenssphären so tief als möglich erkannt haben soll, zu begreifen vermag, muss zugeben, dass selbst der relativ beste Arzt (denn einen absolut guten kann es ja nicht geben) ohne Griechisch, ein noch viel besserer sein würde, wenn ihm dieser unschätzbare Vorzug der höheren Ausbildung vor dem gemeinen niederen nicht abginge.

A. Rose.

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PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

May 1, 1905.

Analysis of 221 Cases of Typhoid Fever. Dr. W. L. Thompson, Worcester, Mass.

The epidemic had started among workmen in one of the suburbs of Boston, and was traced definitely to a privy infection. The cases were treated at the Boston City Hospital. The majority were males and ranged in age from 8 to 63. Sixty-five per cent were in the first three decades of life and five per cent gave a history of previous attack. A motley array of symptoms was seen at the onset, but deafness was initial in 3 cases. The febrile period varied from 7 to 86 days and relapses occurred in 21 cases. Rose spots were present in 69 per cent, sweats were a striking feature in 2 cases, and herpes was noted in 1 case; 23½ per cent showed a subnormal leucocyte count. Myocarditis was marked in 2 cases, thrombosis was seen in 7, infarct of the lung in 1, and parotitis in 2. Nausea and vomiting were troublesome in 5. Hemorrhage occurred in 22 patients, distension was marked in 23, and in 2 cases perforation occurred—both fatal. The spleen was palpable in 69 per cent of the cases noted. True catarrhal jaundice was present in one case. Four showed epistaxis, 3 pleurisy, and 7 bronchitis. The ear was most often affected of the special sense organs. Retention of the urine occurred in 6 cases, acute nephritis in 2. Cystitis was seen three times, hematuria twice. Two patients showed acute mastitis. One patient went to term normally during the disease and was delivered without event. Necrosis of the nasal septum was seen once. The Widal reaction was positive in 93 per cent of the cases noted. The mortality of the series was 12 per cent. The features exhibited by the cases were the frequency of a typical typhoid state, the notable implication of the central nervous system, and the inefficiency of sponging as compared with treatment by tubs.

Painful Heels. Dr. Baer.

Dr. Baer reported 5 cases of this condition. The first was a man of 18 who had had gonorrheal urethritis three months previously and whose discharge was still present on admission. Both heels were extremely painful, no flat-foot was present, and the radiograph showed exostoses beneath the os calcis on both sides. They were both removed by operation and cure was complete. The second patient complained of pain in heels and ankles. There was history of an attack of gonorrhea 9 months previously. The os calcis was found thickened but the patient refused operation. In the third case there was pain in the heels and back. The patient had had three attacks of gonorrhea. There was a spot of extreme point tenderness at the attachment of the plantar fascia. The exostoses were removed by operation, and though cultures were negative the sections showed diplococci which decolorized by Gram. The fourth patient denied gonorrhea but had had an inguinal bubo. Pain in the heels had been present for several months. There was tenderness on pressure over the heel and on stretching the plantar fascia. The radiograph showed exostoses. These were removed and a pure culture of the gonococcus grown from them. In the fifth patient exostoses were removed but were sterile on culture. Operation, however, gave complete relief.

The primary seat of the deposit in these cases seemed to be in the plantar fascia, from which there was a downgrowth into the periosteum. The exostosis was always situated at the attachment of the plantar fascia, but in some of the cases there was also thickening of the sides of the os calcis. Motions were not limited, but there was a characteristic gait, the heels being used little or not at all. When the spine was affected the symptoms were those of an osteo-arthritis. In the two cases in this series in which the spine was affected as well as the heels, gonococci were found in the growths removed from the heels.

Atheromatous Cyst of the Scrotum. Dr. Churchman.

The patient was a colored man, aged 41. The tumor had been present since early boyhood. It lay in the raphe of the scrotum, was freely movable under the skin, and was a little larger than the testicles, though resembling them in shape. It had no definite pedicle. There were no symptoms accompanying it. The tumor was removed under cocaine and proved on section to be an epithelial-lined cyst containing cholesterin crystals and epithelial cells, but no true dermoid elements.

Bladder Calculus in an Infant. Dr. Churchman.

The patient was a male, 19 months of age. He was healthy and sturdy, but had had for four months hematuria with straining pain at stool and on micturition. By means of a small searcher a stone was located in the bladder. The patient had not yet been operated upon. No case of stone in the bladder in so young a patient had occurred in the 80 cases seen at the Johns Hopkins Hospital.

Congenital Urethral Stricture. Dr. Churchman.

This patient was a boy, aged 13, who had come to the clinic complaining of hematuria and pain over the ureter with nausea and vomiting. Previous genito-urinary trouble was denied. An X-ray picture and examination of the urine for tubercle bacilli were negative. Examination of the urethra showed a pin-point meatus and two narrowings—one in the bulbo-membranous portion and one just back of the meatus. Under gradual dilation all symptoms disappeared and the urine became absolutely clear. (See a fuller description in this number of the Bulletin.)

Traumatic Atrophy of the Testicle. Dr. Churchman.

The patient was a man aged 19, who had been normal in every way until 11 months before admission, when he had received a kick in the scrotum, followed by redness and swelling of the left testicle. The swelling soon went down and atrophy then supervened, the testicle gradually shrinking until it reached the size of a hazel-nut. It, with an accompanying varicocele, was removed under cocaine. Section of the testicle showed a good many normal tubules and a few atrophied ones. There was no connective-tissue increase. The vas and epididymis were patent and no good pathological explanation was found for the atrophy. The specimen also contained a curious gland-like structure which looked on cross-section much like the uterus. It was connected with the tunica albuginea by a tube lined by columnar ciliated epithelium which looked a good deal like the Fallopian tube. The structures were thought to be rests of the Müllerian duct.

NOTES ON NEW BOOKS.

Scientific Memoirs by the Officers of the Medical and Sanitary Departments of the Government of India. New Series, No. 14. On a Parasite found in the White Corpuscles of the Blood of Dogs. By Capt. S. P. James, M. B. I. M. S. (*Calcutta: Office of Superintendent of Government Printing, India, 1905.*)

After reviewing the meager literature which refers to protozoan parasites in the leucocytes of birds, the author proceeds to describe a parasite which he found in the leucocytes in the blood of six out of forty-five dogs. These bodies are bean-shaped or rounded structures contained within the leucocytes which seem not to be injured by their presence. Two types may be seen—those with all the chromatin contained in the nucleus, and those with a micronucleus or centrosome situated at the pole of the body opposite the nucleus.

Such parasites are rarely found free in the plasma although one was seen to leave the leucocyte in the form of a vermiculus, which, however, made but slight movements.

This is regarded as a hitherto unknown form of mammalian blood infection and the parasite is named *Leucocytozoon canis*. No fever accompanies even intense infections with the parasite.

Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India. New Series, No. 13. Oriental or Delhi Sore. By Captain S. P. James, M. B. I. M. S. (*Calcutta: Office of Superintendent of Government Printing, India, 1905.*)

In a large proportion of the cases diagnosed as Delhi sore the author found a minute parasite usually enclosed in considerable numbers within large mononuclear cells which form the characteristic feature of the granulation tissue in the floor of the ulcer. These parasites are oval or round; they contain a large nucleus and a second small chromatin mass, sometimes two small ones. Occasionally evidences of division are seen and rosette-like segmentation forms are sometimes found. Inoculation into dogs gave no result, but auto-inoculation has been observed in human beings.

In India, where this condition is common, puncture of the spleen in persons with enlarged spleen failed to show the presence of any such parasites, while in Assam, where the *Kala azar* prevails, in which parasites morphologically identical with these are obtained by puncture from the spleen, nothing resembling Delhi sore which shows the parasite occurs. Probably, therefore, the parasites in these two conditions, while very similar, are not identical.

Publications of Cornell University Medical College. Studies from the Department of Pathology. Vol. IV. (*New York City: 1904.*)

The volume consists of a collection of reprints of papers which have appeared in various journals.

The first, by J. M. Polk, deals with a study of the variations in the hæmolytic power of human serum in varying diseased conditions.

Two papers by Ewing follow, in which he attempts to show that the bodies described as the ætiological factor in vaccine and variola are probably cellular degeneration products.

The paper of Buxton and Vaughan on agglutination is devoted to a study of agglutinins—the agglutinating bodies in the serum, agglutinums—the agglutinable substance of the bacilli, etc. They conclude that in estimating the agglutinating value of a serum one must take into account the agglutinable value of the bacilli. Agglutinoids are agglutinins changed by heat, which will also split off agglutinums from bacilli as free receptors which are probably identical with precipitums.

The next paper, by J. C. Johnston, on Melanoma, refers the melanotic tumors to an endothelial origin except for a few which spring from epithelium.

Other papers follow upon the Chemistry of Malignant Growths, the Psychological Action of Azoimid, Aberrant Thyroid Tissue, Myxœdema and Various Pathological Lesions of the Central Nervous System.

Such a book, made up of heterogeneous papers, all of which have appeared in accessible journals, ought to be convenient for the workers in that laboratory. At any rate, it displays to advantage the activity of the laboratory.

The Surgery of the Heart and Lungs. A History or Résumé of Surgical Conditions found therein, and Experimental and Clinical Research in Man and Lower Animals, with Reference to Pneumonotomy, Pneumonectomy and Bronchotomy, and Cardiotomy and Cardiorrhaphy. By Benjamin Merrill Ricketts, Ph. B., M. D., Member Am. Med. Assn., etc. (*New York: The Grafton Press, 1904.*)

The book, consisting of 510 pages, is divided into two parts, the Surgery of the Heart and the Surgery of the Lungs, and at the beginning of each the terminology used in that part is given, which is convenient to the student. There are 177 pages of bibliography, and each chapter is followed by the literature of its own particular subject, which is a good arrangement. A large number of the remaining pages are taken up with historical notes and extracts from papers mentioned in the bibliography. Research work on the heart and lungs of dogs occupies about 50 pages, and some of the original experiments are interesting. The illustrations are excellent, being either photographs or photomicrographs. The practical hints on suturing, drainage, and other points in technique are useful.

On the whole the book will probably be much more interesting to one requiring references to the literature than to the practical surgeon, because some of the most successful methods of operation are not considered, among others the use of Sauerbruch's air chamber.

A Treatise on Diseases of the Nervous System. By L. Harrison Mettler, A. M., M. D., Associate Professor of Neurology, College of Medicine of the University of Illinois. Complete in one volume. Profusely illustrated; two color plates; full indexes; pp. 990. (*Chicago: Cleveland Press, 1905.*)

This is a ponderous volume of nearly one thousand pages, devoted to an extended and rhetorical description of nervous diseases based upon the neurone doctrine. A "provisional classification" is introduced which the author states may be subject to change from time to time. Briefly it is as follows: I. Neuronic Diseases (Parenchymatous Degenerative Troubles). (a) Functional, (b) Organic. II. Non-neuronic Diseases (Interstitial and Vascular Troubles affecting the Neurones secondarily). III. General Intoxications with Special Nervous Symptoms.

This innovation will hardly meet with general favor, as the old system of classifying diseases into those of the Brain, Spinal Cord, and Peripheral Nerves has been in use for many years and has proven satisfactory. The dogmatic statement that "the neurone doctrine is now an accepted fact" is certainly questionable in the light of recent investigations. The book shows wide reading and hard work in its preparation. It treats exhaustively the various diseases—in fact, there is a verbosity about many of the chapters that might well be omitted.

Modern psychology is used freely to explain many "psychophysical" manifestations. In reading this work there are several omissions that are very striking. For example, under Tabes no mention is made of hypotonus and but brief reference to Frenkel's systematic exercise treatment. Babinski's sign is described, but no statement is made concerning its special significance, and under Spastic Paraplegia it is not given as one of the symptoms, nor is ankle clonus referred to, both of which are very characteristic of this disease. The chapter on Cerebral Localization embraces thirty-five pages devoted largely to the psychological aspect of the subject. There is only one illustration of this important section. The pathologic changes in the cortex in general paresis are briefly touched upon and then not in accord with the recent views of Alzheimer, Nissl, and others. The chapters on epilepsy are drawn largely from Spratling's recent book. There are so many other text-books on neurology more concise, practical, and accurate that it is difficult to see just the place such a book as Mettler's will fill. The illustrations are profuse and well selected. Those from Held, Spalteholtz, and Jakob suffer in clearness of detail from reproduction. The print is clear and the paper good. The general make-up of the book is first class. A. P. H.

The Ophthalmic Year-Book. A Digest of the Literature of Ophthalmology, with Index of Publications for the Year 1903. By Edward Jackson, A. M., M. D. With 45 illustrations. (*Denver: The Herrick Book and Stationery Co., 1905.*)

This book contains an excellent digest of the best contributions to ophthalmic literature for the year 1903. The editor's work has been well done, and his judgment of the real worth of contributions to ophthalmology for that year is excellent. By the omission of much trivial and unimportant matter, the editor has been able to extract and direct the better articles appearing in that year with sufficient fulness to be of real value to the practitioner. The general arrangement of the digest of subject matter is very good, and a very clear idea of the newer views held regarding the pathology of various affections of the eye may be obtained from its pages.

The book on every page shows that the author has gone over the literature for the year 1903 with care and judgment. There is a very convenient reference table to the literature for that year in the back of the book. B. B. B.

Atlas and Epitome of Operative Ophthalmology. By Prof. Dr. O. Haab, of Zurich. Authorized translation from the German with editorial notes and additions. Edited by G. E. de Schweinitz, A. M., M. D., Professor of Ophthalmology in the University of Pennsylvania. With 30 colored lithographic plates and 154 text cuts. (*Philadelphia, New York, London: W. B. Saunders & Company, 1905.*)

This is the third and last atlas on ophthalmology in the series of medical hand atlases published by the Saunders Company. The color plates are good, and serve to illustrate the text very well. Unlike most atlases, which seem to exist chiefly for the edification of the eye, this book possesses much merit in its text, for the description of the various operations for the relief and cure of many diseases of the eye are so clear and full that the volume can well hold place with more pretentious text-books on the eye. The author enriches the book with numerous practical and important details which his long clinical experience has taught him to be of importance for the complete success of the operations described.

The book can be well recommended to the specialist, practitioner, and student as an excellent exposé of operative ophthalmology at the present day. B. B. B.

A Compend of the Practice of Medicine. By Daniel E. Hughes, M. D. Seventh edition. Revised by Samuel H. Brown, M. D. 779 pp. (*Philadelphia: P. Blakiston's Son & Co., 1905.*)

This posthumous edition of the late Dr. Hughes' work is considerably augmented in size, though the thin paper and flexible covers make it a handy volume.

As a compend for quick reference the book has a definite value, as the subject matter is presented in a clear manner with the salient points and differential diagnoses emphasized. There are also sections on clinical methods and modern therapy.

T. R. B.

The American Year-Book of Medicine and Surgery. Edited by George M. Gould, M. D. Medicine. (*Philadelphia and London: W. B. Saunders & Co., 1905.*)

We have from year to year expressed our appreciation of this publication. The volume for 1905 keeps up the high character of its predecessors. In his preface Dr. Gould notes that there is one change in the editorial staff owing to the death of Dr. S. W. Abbott, of Boston. His department, that of Public Hygiene and Preventive Medicine, will in the future be in the hands of Dr. John S. Fulton, of Baltimore. The extracts throughout the volume seem to have been done with the same care as formerly. As Dr. Gould notes, there is increasing difficulty in keeping down the size of the volume.

The International Medical Annual. 1905. Twenty-third year. (*New York: E. B. Treat & Co.*)

This publication shows signs of prosperity, as the size of the page has been increased. Despite this the price remains the same. This volume opens with a careful review of the more recent advances in therapeutics. In the discussion of various subjects special attention is paid each year to certain subjects. Thus the surgical treatment of Bright's disease, various gastric and intestinal conditions, diseases of the pancreas and of the prostate re-

ceive special mention this year. There are two good colored plates showing trypanosomes and Leishman-Donovon bodies. There are a number of plates illustrating eye conditions.

We can only repeat the favorable opinion expressed in the past regarding this work. It is extremely useful, especially for the busy practitioner who wishes to have recent advances in a form which is easy of reference and reliable. There are many references to the literature of the past year.

Bacteriology and Surgical Technic for Nurses. By EMILY M. A. STONEY, Superintendent of the Training School for Nurses, etc. Second Edition. Thoroughly revised and enlarged by FREDERICK RICHARDSON GRIFFITH, M. D. (University of Pennsylvania). Illustrated. (*Philadelphia, New York, London: W. B. Saunders & Company. 1905.*)

A previous edition of this book was noticed in the BULLETIN some time ago. The present edition contains all the merits of the former and has been much improved by a thorough revision and the addition of more than 80 pages of letter press. The glossary at the end of the book is more apparent than real, being much too restricted and should be much enlarged in a future edition. Why emesis, for example, should be included and enuresis omitted or why actinomycosis should be defined and acetonuria omitted are queries which cannot be satisfactorily answered. A glossary to be of any value should include words which are liable to be encountered by the nurse in her reading. It is not sufficient to define a few ordinary words the meaning of which should be known to every tyro in nursing.

The Effects of Tropical Light on White Men. By MAJOR CHAS. E. WOODRUFF, A. M., M. D., Surgeon U. S. Army. (*New York: Rebman Company; London: Rebman, Limited, 1905.*)

The former publications of Major Woodruff on anthropological subjects have attracted wide attention and excited much discussion. It can hardly be thought that the contention in the present volume will pass unchallenged. The author believes that zoological zones exist upon the surface of the globe which are best suited to the living, and development of individual races of men. He believes for example that blonds are best suited to the temperate zones, yellow men to the sub-tropical regions, and black men to equatorial countries and that any attempt on the part of either of these three colors to invade the natural habitat of the other is followed by disaster. He believes that the important agent in producing the physical and nervous degeneration of the blond is light which at first stimulates and later destroys the vitality of races which are not protected from its injurious effects by a pigment in the skin. His theory is that the blond is probably the highest type of race and is capable of higher performances than any other under normal conditions of climate, but that invariably when the blond has attempted to invade the tropics he disappears because he is not adapted to a tropical existence.

The author brings a wealth of historical material to support his theory and presents it in an interesting way.

The practical application of the book to our recent occupation of the Philippines and West Indies is obvious in a chapter on "Practical Rules for White Men in the Tropics," which should be carefully considered by all who have to do with our new possessions. The book is attractively gotten up and should have wide circulation.

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CONTENTS.

	PAGE
Surgical Physiology. By George W. Crile, M. D.,	269
A Needle and Clamp for Injecting Lymphatics. By William Snow Miller, M. D.,	273
Marcello Malpighi. 1628-1694. By W. G. MacCallum, M. D.,	275
Typhoid Appendicitis without other Intestinal Lesions. By William Royal Stokes, M. D., and Albert L. Amick,	284
The Pathological Anatomy of Exophthalmic Goitre. By W. G. MacCallum, M. D.,	287
Proceedings of Societies: The Johns Hopkins Hospital Medical Society,	288
Clinical Features of Thyroid Hypertrophy [Dr. Halsted];—The Pathological Anatomy of Exophthalmic Goitre [Dr. MacCallum];—Bacteriological Observations in Some Cases of Bronchiectasis [Dr. Boggs];—Acute Pericarditis in Pneumonia [Dr. Chatard];—A Study of the Physiological and Toxicological Actions of the Toxic Agent of Pneumonia. Therapeutic Observations and Indications [Dr. Brem].	
Notes on New Books,	289

SURGICAL PHYSIOLOGY.[1]

By George W. Crile, M. D.,

Professor of Clinical Surgery, Western Reserve University, Cleveland, Ohio.

In the earliest period of its development surgery was wholly empiric. The period of gross anatomy which followed gave rise to a splendid development of the mechanics of surgery, a development that long ago reached its zenith. Gross anatomy led to the unfolding of minute anatomy and pathologic anatomy. Upon this foundation was erected the splendid structure of surgical pathology and bacteriology. Previous to this time surgery, like law, was taught and practiced largely by precedents. Surgical pathology and bacteriology transformed the old anatomic surgery. The approximate causes of the majority of the surgical diseases are now known, or correlated, but what can we say as to the development of our knowledge of the vital processes of surgical importance? We know the gross and the minute appearance after death. What knowledge have we of the physiologic alterations leading up to death or to recovery, or of the wonderful scope and method of compensation in injury and in disease, or of the local and of the general resistance toward infection?

Anatomy, pathology, and bacteriology contribute a scientific basis, a house from which an inference as to the life history of its previous inhabitants may be drawn.

Surgical practice rests largely upon altered physiologic actions, or upon surgical physiology. As illustrations let us consider a few of the simplest phases of the surgical physiology of operative surgery as relates to two of the most vital phenomena—respiration and circulation.

With the definite knowledge that in respiratory obstruction respirations are not immediately arrested, but are stimulated in force, though not in frequency, and that in mechanical stimulation of the laryngeal mucosa there is usually an immediate respiratory arrest, there should not be a moment of doubt in differentiating between reflex inhibition and obstruction, thereby avoiding certain crises in the extraction of foreign bodies or in performing intubations. When there is threatened asphyxia from the pressure of tumors, requiring the aid of the accessory muscles of respiration, with the knowledge that these muscles are voluntary and are paralyzed by general anesthesia, the too frequent catastrophe of sudden death from paralysis of these muscles could not occur. In administering

[1] Read before the Johns Hopkins Hospital Medical Society, March 20, 1905.

anesthetics, were students in the physiologic laboratory made familiar with the respiratory arrest caused by pulling the tongue forward too forcibly and swabbing the region of the epiglottis, the vicious circle of greater effort, causing more inhibition, and the increased inhibition inducing the anesthetizer to greater stimulation of the inhibitory area of the throat, would cease to be an incident in the earlier experience of the hospital interne. The markedly increased respiratory action caused by the manipulation of certain areas, as divulsion of the anus, deep manipulation in the pelvis involving the sigmoid and the rectum, extensive manipulation of the peritoneum, causing a temporary increase in the exchange of air and equally of the anesthetic, especially in the case of chloroform, has produced dangerous collapse and even death.

Manipulations of the peritoneum, if rough and considerable, especially in the neighborhood of the diaphragm, as so often noted in stomach and gall-bladder surgery, produce a reflex excitation of the abdominal expiratory muscles, and often cause an expulsion of the intestines through the incision. Appreciation of this purely reflex physiologic phenomenon would prevent the anesthetizer from trying to anesthetize it away, under the impression that the patient was coming out from the anesthetic, neither would the surgeon institute the vicious circle of increasing the reflex expulsive force by roughly manipulating the intestines in trying to force them back, causing an equal increase in the expulsive contractions.

In peritonitis the surgeon would note that the abdominal factor of respiration is eliminated and that the superior costal type of respiration is substituted, and that since only the upper parts of the lungs are being used, the respiratory exchange must be the more rapid to compensate for its shallowness, that the scaleni and the levatores on palpation show greatly increased action, that the upper chest excursions are greatly increased in amplitude, and that the lower chest is even and flat. These phenomena are but physiologic inhibitions and compensations, and are of high diagnostic value.

The surgical physiology of the circulation is more vital than that of the respiration. The control of the circulation often means the control of life itself and constitutes the most important factor in the immediate operative results.

Physiology has shown that quite independent of general anesthesia the manipulation of any sensitive tissue sends impulses to the vasomotor center, modifying it in a physiologic sense, and that if these impulses are strong enough or numerous enough, this center becomes functionally impaired, and that this impairment may be sufficient to render the center wholly inactive. *Pari passu* with the development of this functional impairment the blood-pressure falls. The lower blood-pressure then becomes a factor in the further impairment of the vasomotor center by diminishing its nutrition. When the center has reached a state of complete functional dissolution it cannot be restored by its own action, since it is no longer excitable.

A knowledge of the definite physiologic laws governing this state would always guard the surgeon against excessive manipulation, would spare the patient the extra stress of therapeutic stimulation, and would lead the surgeon to support the circulation by mechanical means, such as saline infusions, posture, bandaging, or better still the rubber pneumatic suit. It would also lead him to secure the rest required for restoration.

The respiratory and the vasomotor centers are especially dependent upon a certain blood-pressure for their functionation. Note some of the powerful compensating mediums for maintaining the required blood-pressure. When there is an increased intracranial pressure from abscesses, hemorrhage, tumors, etc., a marked resistance to the intracranial circulation arises, threatening the nutrition of these centers. At once the vaso-constrictor impulses are sent out, especially to the splanchnic area. The blood-pressure rises to overcome this, hence the hard pulse and the high blood-pressure so characteristic of increased intracranial pressure.

How many times has this pathologic pulse misled the unphysiologic surgeon to a false security? How often has such a patient, whose compensating mechanism has been taxed to its utmost, been given full anesthesia, especially chloroform, causing just a sufficient fall in the blood-pressure to produce a sudden arrest of respiration and soon after of the circulation as well?

The simplest proposition in physiology is the slowing of the pulse and the rise in the blood-pressure in asphyxia. The pulse is increasingly slowed until the moment of death in asphyxia, yet how often have surgeons made a fatal misinterpretation.

The reflex inhibition of the heart from mechanical stimulation of the trunk of the superior laryngeal nerve or its terminal in the mucous membrane, in operations upon the larynx, such as laryngectomies, and intubations, causing the sudden collapse, even death, would, if its physiologic significance were understood, almost never occur.

The abdominal cavity bristles with circulatory reflexes. Each contact, every exposure, is a factor. The result of an operation is the sum total of all the contacts and of all the exposure. The total physiologic expense of a given abdominal procedure by one surgeon may be multiplied in the hands of another. In certain operations upon the extremities, the immediate effect may be totally obviated by the employment of a physiologic "bloc" of cocain, a procedure just as important in general anesthesia as in local. For example, operations for the excision of the shoulder girdle by "blocking" the brachial plexus may be done shock free, excepting for the minor part, represented by the division of the parts not supplied by the brachial plexus, a rather small factor.

In deep anemia, in infections, in cachexias, etc., the potential energy of the vasomotor centers is lowered. One must make a physiologic invoice of the amount of vital energy available and plan to operate within that limit. For example, in the case of acute infections, such as acute cholecystitis, large collections of pus in the abdomen of tubal or appendicial origin, leaving only a fraction of the normal physiologic margin for bearing the stress of the operation, how much safer it is

to merely open the abscess under morphin-cocain or nitrous oxide-oxygen anesthesia within the physiologic limits of safety at that moment, then, as the patient rallies, if further drainage is required, a wider physiologic margin has been acquired and a more extended operation may be performed. Finally, after the entire acute process has been safely passed, a complete clinical cure by the regular procedure may with safety be adopted. That is to say, many surgical diseases are most safely treated by an operative physiologic progression.

The field of referred pain in diagnosis is one of the most fruitful in the surgical borderland of physiology, yielding, especially in the visceral lesions, the most individualizing groups of subjective symptoms known. Recent investigations have shown that perhaps the most important circulatory changes in the acute infections are of vasomotor origin. The more accurate blood-pressure records obtained by the sphygmomanometer not only show this but they also indicate some characteristics of individual infections. Typhoid infections lower the vasomotor action, and so the blood-pressure. On the other hand, the staphylococcus, streptococcus, and colon bacillus infections cause a marked rise. This antithesis has proven of importance in the diagnosis of typhoid perforation. The blood-pressure in certain acute infections is raised by a stimulation of the vasomotor center. The futility, or may we not say the harm, of using drug stimulation in addition to the powerful toxic stimulation, must be obvious.

Consider the main facts of the circulation in acute peritonitis. The pulse is small and hard—small because a large amount of blood is localized in the splanchnic area, a regional intravascular hemorrhage—and hard because the vasomotor centers are stimulated, causing an increased blood-pressure; that is to say, the splanchnic area is flooded, the somatic area is drained. The face becomes a composite photograph of hemorrhage, pain, and infection.

A matter of surgical importance and one of the most admirable attributes of the human vital force is the physiologic compensation of one part or organ for another.

One muscle may compensate for another or a group, and a part for the whole; the loss of bones or joints may be compensated for by minimizing some functions here and exalting others there; a portion of one lung may compensate for both; one kidney, for the other. In laryngectomy, the mouth finds new vocal cords. In gastrectomy the stomach function is assumed by the intestines, and for the loss of the greater part of the latter, compensations have been provided. The rectum may act for the bladder; the abdominal muscles for a sphincter ani. Ductless glands and bone marrow reciprocate in times of physiologic distress. The range of compensation in injuries and diseases of the heart, by virtue of the compensatory assistance of the great thoracic pump, the respiratory system which alone is capable of producing a moderate circulation, is as yet scarcely considered. Note the quickened circulation, increased respiration and reabsorption of tissue fluids in compensation in acute hemorrhage. The loss by occlusion of the largest arteries and veins may be quickly met by the combined compensatory effort of innumerable smaller vessels.

The foregoing are only a few crude examples among the compensations well known, while innumerable ones of infinite delicacy and balance and vital importance are still unknown.

It is truly difficult to handicap an organ beyond some compensation, or to physiologically incapacitate a vitally strong man.

The Problems of Surgical Physiology.—Turning now to the problems of surgical physiology, what are they, or rather, what are they not? Among the many obvious ones we may recognize the general or the fundamental and the more specialized. Among the fundamental problems is that of knowing more definitely about that interesting property of protoplasm by which it is, in a measure, able to overcome changes in its environment; as, for example, the protoplasmic response to foreign bodies in the tissues, to various stimuli, to altered nutrition, to the effect of various drugs repeatedly administered, to changes in temperature, etc. Instead of surgical empiricisms along this line, could not some fundamental laws be established enabling us to utilize the range of protoplasmic adaptability to surgically modify, or to protect the functions? It would seem that the range of protoplasmic adaptability is at its height when the change in its environment is due to an infecting organism. In their Titanic struggle toward discovering the nature of the physiological response of tissues to infection, pathologists have turned more than half physiologists, and in this dual rôle, may we not hope they soon will solve the greatest problem in surgical physiology.

In the general problem of hemorrhage there has not, to my knowledge, been adequate investigation of the irreducible minimum of nutrition and oxygen for the survival of the various tissues and organs, since death in no two organs is produced by like conditions; for example, while a skeletal muscle may for hours be deprived of its active circulation, then resume its function with the return of the circulation, the highly specialized centers in the medulla can not, perhaps, endure a lost circulation beyond half an hour.

A splendid field for investigation would be the determination of the most practical methods of artificially prolonging the functional activity and the life of the various tissues and organs to tide over surgical crises. The reverse of this picture is also true; do we know enough of the real status of blood-letting in certain infections and poisonings? Has the action of drugs been sufficiently studied in the various grades of hemorrhage? Is the medicinal dose the same whether all the blood, or only half of the blood is in the circulation? If the effects of the drug bears a ratio to the amount of blood rather than the weight of the body, is it reasonable to give the same dosage in profound hemorrhage as when the normal quota of blood is present? The lymphatic circulation with reference to malignant metastases and infections, as recently emphasized by C. H. Mayo, is an important field.

The important problem of the surgical physiology of thrombosis and embolism has been scarcely touched.

The problem of surgical shock has been only opened, but the meager information thus far gained has already helped to throw some light upon certain immediate phenomena attending surgical operations. Physiologic chemistry should soon permit us to sustain life over crises by subcutaneous feeding.

Specialized Problems.—Among the more specialized problems the surgery of the brain presents probably the most intricate. While tremendous strides have been made in the surgical physiology of this organ, the future will no doubt show much further elaboration of the localization of the motor areas, of the physiologic adaptability of the respiratory and circulatory centers. It would seem that the accumulating surgical experience as well as the researches upon the higher brutes should lead to a possible localization of certain mental and psychical mechanisms whose representation in the brain may have localizations akin to that of motor representation. What a splendid problem is that of the investigation of the change in metabolism in tumors and injuries of the pituitary bodies. Should we not make a thorough investigation upon the medulla to discover whether or not the operative field in the base could not be extended by cocainizing the medulla and artificially maintaining the circulation and the respiration during an operation in this region, thereby protecting these centers from the numberless impulses caused by the operative trauma, tending to produce functional destruction of these centers? May these centers not be protected by cocainization until the stage of danger is passed? Would it not be possible to prevent the destructive post-operative stimuli arising from the exposed, newly-made raw surfaces by such procedure, thereby minimizing the progressive accumulation of destructive stimuli; that is to say, is it not possible to effect a functional detachment of the medulla conferring something of the degree of immunity enjoyed by the vital centers of reptilians?

In this field so much brilliant work has been done in recent years by such men as Horsley, Sherrington, Cushing, and others that it is not too much to expect still greater developments.

In the operations upon the neck we are greatly in need of more knowledge of the physiologic importance, as well as the range of possible compensations of every muscle and nerve and gland involved. We need to know, too, much more about the matter of thrombosis occurring after ligatures of vessels such as the external carotid. We also need to know more definitely about the requirements of a sufficient cerebral nutrition in the various stages of life, so that we may be more accurate in our judgment as to what patients may be subjected to a permanent closure of the common carotid artery without causing cerebral softening.

In the surgery of the thorax we have just begun to know the important problems in the surgical physiology of the heart and of the lungs. Even by our present crude methods we know that the heart may be stilled and be made to beat again almost at will. I have been able to cause a resumption of the heart beat in which there was a demonstrated cessation of circulation varying from six to twenty-four minutes. In two, the circulation and respiration resumed their automatic rôle again. In one other the respirations were not established in good rhythm. Three of these cases were suicides by drowning, two were cases of extensive crushes of the skull involving mass destruction of the brain, one occurred in the course of an operation for an extreme case of exophthalmic goitre, one while attempting to remove a tumor of the cerebral base.

With the further elaboration may we not be able to overcharge the blood with oxygen and instantly stop the heart by an electric inhibition, perform an operation upon an obstructing aortic valve, then promptly set the automatic mechanism of the heart in motion again? Even at present one might have ten minutes' grace at one's command for the execution of a cardiac technique upon a quiescent heart.

Then, again, by dint of great practical familiarity with every physiologic phase of that most persistent automatic muscle, we must, in preparation for such work, divest ourselves of the ancient and almost superstitious dread of the heart. An organ that will beat rhythmatically and do light work two days after conventional death, is entitled to more surgical confidence than has been accorded to it. I have been able to maintain a continuous rhythmic cardiac action and a complete circulation of the blood for a period of eleven hours in an animal whose medulla was detached by decapitation. Our practical knowledge of the pulmonary circulation as affecting the systemic circulation is, in our practical work, infantile. The profound impression upon the cardiac circulation by altering the intrapulmonary pressure is equal to the effect pressure upon the aorta would have upon the cerebral circulation. The Sauerbruch apparatus, as I understand it, was originally proposed with reference to the question of the collapse of the lungs, when in fact the greater risk of opening the chest is a circulatory one. The maintenance of an exchange of air on the physical principle of varying intrapulmonary pressure which affects the circulation so vitally, has an automatic adjustment so delicate that it will be found extremely difficult to substitute any artificial means. In order to protect the circulation it will be quite necessary to have control of the air pressure in both the pulmonary and the systemic circulations. This, I attempted several years ago, the results of which were published in a monograph on "Blood-Pressure in Surgery." I found that no means at my control enabled me to maintain the balance of circulation on a safe basis.

Were it possible to have the pulmonary and the systemic circulations under two separate atmospheric pressures of such delicate and efficient adjustments as to make a working substitute for the vasomotor center, a marvelous mechanism for the vital management of the circulation and life itself might be constructed.

We have seen how blocking of the nerve trunks excludes shock in operations in the regions supplied, permitting us, for example, to make an interscapulo-thoracic amputation without shock. Following this use of cocain we made a series of experiments by injecting cocain directly into the spinal cords

of frogs and dogs. We found that this block was just as effective as in the nerve trunks. The physical damage, however, prevented the application of this method clinically, excepting in such cases in which the importance of damage to the cord is eliminated. My associate, Dr. Lower, and myself were for some time hoping for a suitable case of crushing of both lower extremities requiring double amputation through the thigh. This opportunity came to Dr. Lower, who in 1898 injected the spinal cord itself and made a double amputation of the thigh without the use of general anesthesia. There was no shock and no pain, the patient making a good recovery. This is mentioned in order to call attention to the splendid possibilities of research on cataphoresis of the spinal cord. If a dentist is able by this means to anesthetize an entire dental nerve, may it not be possible to elaborate a technique whereby a cocain block may be applied to the spinal cord without any contact with this organ? The use of insulating needles would at once suggest itself. If such blocking could be established, the entire peripheral field would not only be anesthetized but rendered shock-proof as well.

The abdominal cavity is fairly distended with interesting problems in surgical physiology. The illuminating researches of Pavloff, the recent work of Cannon and others, should all be translated to the operating room in the surgery of the stomach and intestines. The problem of gastric surgery has been only opened. The physiologic disturbances incident to the operation leading to vicious circle and other complications must be more definitely solved by a better study of its surgical physiology. The infections, obstructions, and numerous fields remain unsolved.

In passing, we need only mention the supreme importance of the surgical physiology of the thyroid, the pituitary, and the suprarenals.

The surgical physiology of the kidneys is an important field.

We have in this brief outline sketched a few of the problems in surgical physiology. Anyone wishing to work in this field will not be confronted with the question what to do, but with the question what not to do. The field is limitless and has scarcely been opened.

I cannot do better than to close with Hektoen's quotation of Virchow's prophetic utterance, published in 1847: "The standpoint we aim to occupy is simply that of natural science. Practical medicine, the applied theoretical, the theoretical pathologic physiology, is the ideal we shall strive to reach so far as our powers permit. While we recognize fully the title and the independence of pathological anatomy and of the clinic, they serve us pre-eminently as sources of new questions, the answers of which fall to the lot of pathologic physiology. Inasmuch, however, as these questions to a large extent may be formulated only through painstaking and comprehensive detailed study of manifestations of disease in the living, and of the conditions in the dead, we regard the exact growth of anatomic and clinical experiences as the first and most important demand of the present time. From an empiricism of this kind will result gradually the true theory of medicine, pathologic physiology."

A NEEDLE AND CLAMP FOR INJECTING LYMPHATICS.

By William Snow Miller, M. D.,

Associate Professor of Anatomy, University of Wisconsin.

Various aids have from time to time been devised by investigators to make the demonstration of the lymphatics easier and to do away with the hap-hazard "puncture method." None of them met the requirements of the problem which presented itself to me in my work on the lymphatics of the lung.

In the lung the superficial lymphatics are quite sizable, more easily recognized in the distended than in the collapsed lung, are thin-walled and are situated in the pleura which is spread out over the surface of the air spaces. Any lessening of tension in the distended lung will permit it to collapse to a greater or less degree, and in so doing will cause the point of an ordinary hypodermic needle to perforate the wall of the lymphatic, or, what is more unfortunate, that of the lymphatic and air space; an accident which prevents any further attempt to inject the lymphatics of that lobe of the lung.

To prevent leaking of the injection mass the needle must be tied in the lymphatic or held tightly between the thumb and fingers. This latter procedure is tiresome, prevents the use of both hands in working, and is generally impracticable; the former is out of the question because invariably the walls of the air spaces are perforated.

The point of the ordinary hypodermic needle is too sharp.[1] This fault leads to perforation or tearing of the walls of the lymphatic and consequent diffusion of the injection; an accident to be carefully avoided for it has led to some egregious mistakes. The patience of the investigator is also often severely tried by the point of the needle being accidentally pushed through the wall of the lymphatic by some slight movement and, although up to that time all has been going well, the injection is ruined.

[1] I made many experiments with capillary glass cannulæ but found them even more impracticable than hypodermic needles.

To obviate these difficulties, I devised in the winter of 1895-96 the following needle and clamp, which has served me in a satisfactory manner ever since.

In planning the device I kept the following points in mind, viz.: the point of the needle should not have the sharp point, so necessary in the ordinary hypodermic needle; the needle should not exceed one millimeter in diameter and the caliber should be as large as possible (instrument makers differ in their expertness in making needles); the needle should be held in place by some means which would not perforate the delicate walls of the air spaces, would prevent leaking of the injection mass, and would also protect the walls of the lymphatic or the air spaces from being perforated by the point of the needle in subsequent manipulations.

Figure 1 shows the form of the needle I finally found best adapted to my use. The point is round, not sharp, and its length is greater than that of the ordinary hypodermic needle. Personally, I prefer, when using a syringe, to connect the needle with the syringe by means of a short piece of rubber tubing. This possesses the advantage of flexibility over a rigid connection and facilitates the use of the syringe. In the illustration the rubber tube is shown much too short.

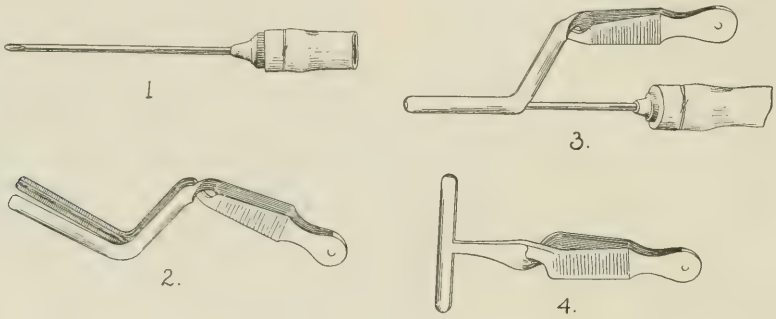
The principal feature of the device is the clamp, which may be made in two forms, as shown in figures 2 and 4. The clamp is a modification of the well-known artery clamp so commonly used in all laboratories. Each arm is hollowed out (figure 2) to correspond to one-half the diameter of the needle so that when closed over the needle it is firmly held, as shown in figure 3. At the end of each arm the groove flares slightly. Of the two forms shown in the illustrations I personally prefer that of figure 2, but in some instances that of figure 4 is best adapted to the place.

The size and proportions of the needle and clamp can be modified to meet the requirements of the investigator. I have illustrated those that were best adapted to my own problem.

When using the needle and clamp the lymphatic is opened by an oblique cut made with a pair of fine, sharp-pointed scissors; then introducing a fine probe to keep the vessel from collapsing, the needle is pushed in beside the probe, which is now carefully withdrawn, and one of the clamps applied in such a manner that the end of the needle is just enclosed by the clamp, as shown in figure 3. The rounded end of the needle allows it to slide along the probe easier than a sharp point and there is almost no danger of perforation during its introduction. The advantage of the flare at the end of the groove is now seen; the end of the needle is enclosed by the clamp, but the injection of the lymphatics is in no way interfered with, and the end of the needle cannot injure the walls of the lymphatic or those of the air spaces.

I have also used the needle and clamp in injecting blood-vessels, and it has been suggested to me that the device could be used to advantage in certain bacteriological manipulations.

Examples of the work which can be done with the aid of this simple device may be seen in my paper "Das Lungenläppchen, seine Blut- und Lymph-gefässe," in the *Archiv für Anatomie und Physiologie*, 1900, and "The Blood- and Lymph-vessels of the Lung of Necturus" in the forthcoming volume of *The American Journal of Anatomy*.



The figures show the needle and clamp nearly their actual size.

STUDIES IN TYPHOID FEVER.

SERIES I-II-III.

The papers on Typhoid Fever, edited by Professor William Osler, M. D., and printed in Volumes IV, V and VIII of the Johns Hopkins Hospital Reports, have been brought together and bound in cloth.

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Marcellus Malpighius Phil. et Medicus Bononiensis Collegiatus
Olim in Pisana universitate ordinarius medicinę professor Mox in
Messanensi Primarius in Patria demum eandem profitende ad Annum
Aetatis suę 63. a SS. D N Innocentio XII eiusdem sanitatis hę-
le. gratia Romam accitus, ac inter intimos a cubiculo in
Aula Pontificia participantes adscriptus.

MARCELLO MALPIGHI.[1] 1628-1694.

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There is in the history of medicine a remarkable contrast between two types of mind, both of which are represented by great and familiar names. Of these extremes, each of which has nearly always some of the characters of the other, one is made up of those men who, with great personal influence over their fellow-men, use what facts they have at their disposal, or more frequently what convictions are grafted in their minds to construct a theory and from the theory a system of knowledge with an explanation for all difficulties, and a niche even for such as are not yet thought of. Such men were Galen, Paracelsus, Hoffmann, John Brown, Broussais, and many more—men not always without wide knowledge, but who employ rather the deductive method than the inductive. At the other extreme were such as Hippocrates, Vesalius, Harvey, John Hunter, Morgagni, and Malpighi—men who did produce generalizations, but generalizations which were conscientiously based on real facts which they themselves had delved out of nature and which, unlike such systems as Brownianism and the physiological medicine, will last for all time. It is particularly in this character of objective observer, possessed of treasures of fact, before he signed any bond of theory, that Malpighi comes before us to this day as a model. He appeared at an epoch when such giants as Vesalius and Harvey had overthrown the universal confidence in the authority of the ancients—a period when there was suddenly work to do with no appeal to precedent—when the microscope suddenly threw open the enormous field of the minute and invisible, to the searching eye. Letters had fallen to a low ebb—ignorance was vast and overwhelming, and despite the brilliance of the preceding centuries, writers were given over to bombastic ornamentation of their writing, but a few honest and bold spirits turned from authority to nature—exact science arose.

Malpighi was one of the leaders of the movement which tore science from the bonds of tradition and the church, and rendered it independent of the ancient masters who had for so many centuries dominated everything medical.

Marcello Malpighi was born at Crevalcuore, a small town near Bologna, on March 10, 1628. Of his early life nothing is known except that his parents were small landowners who seem to have recognized some ability in their son in sending him to Bologna to study. There he entered the university in 1645 and continued his studies until the death of his parents in 1649, which left to him the care of the large family and of the estate upon which the neighboring family Sbaragli made constant attempts at encroachment. Nevertheless, he resumed his studies next year with the peripatetic philosopher Natali, upon whose advice he took up the study of medicine with Bartolommo Massari and Andrea Mariani. Of these Massari was a diligent anatomist who lost no opportunity of dissecting not only animals but human beings and who formed of his students a small society which met at his house to carry out these dissections. This academy of anatomy, founded in Bologna in 1650, was similar in some respects to the Accademia dei Lincei of Rome, and there being nine students, Massari called it the Coro anatomico in homage to the "coro" of the muses. Among them were Malpighi, Fracassati, Capponi, and Golfieri, and the friendships formed there remained strong through Malpighi's whole life.

At this time the doctrines of Galen and the Arabs still dominated the whole of medicine and teachers merely expounded the works of these authors, sometimes altering them to their great hurt. Malpighi soon appreciated the fact that Hippocrates had been a more accurate observer of nature than those later writers and devoted his thesis to upholding this view with the result that he greatly irritated his masters who, nevertheless, could not withhold their esteem of so brilliant a student.

In 1654, the year after his graduation, he married the daughter of his master, Francesca Massari—as Ferrario says, "assai virtuosa donna ma non ebbe figli." This was a very happy union, although they had no children, and she was his constant companion and support throughout nearly all of his life.

In 1656, when twenty-eight years of age, he was nominated by the Bolognese senate as public lecturer in medicine, three years after his graduation in medicine and philosophy. The liberty to give lectures thus through some animosity withheld from him for a time after his graduation, was granted apparently in connection with Massari's sudden death when he was called to the chair of medicine. In the same year, however, he was requested by Ferdinand II, the grand duke of Tuscany, to come to Pisa, there to give instruction in the science of medicine, and realizing the antagonistic attitude of his own townsmen he accepted the offer.

There in Pisa he dwelt with one Girolamo Barbato and worked happily in the sunshine of Ferdinand's favor and interest. Borelli, the celebrated mathematician and physicist, became his friend, and the two learned much from one another; Borelli teaching him the philosophy of Galileo, while Malpighi in turn imparted his enthusiasm for biological lore and his knowledge thereof. They two (later with Auber, who discovered the tubular structure of the testis), made many dissections, and the dukes and the princes attended and tempered thus the cares of state. Hence arose the famous

[1] Read at the meeting of the Johns Hopkins Hospital Historical Club, January 16, 1905.

Accademia Cimenti, or academy of experiment, which was later transferred to Florence and which, like the Accademia dei Lincei of Rome, numbered some of the most famous men of the times on its rolls.

While at Pisa, Malpighi studied the bullock's heart, macerating and boiling it until he found that the fibers run spirally, and this he at once showed Borelli. Some discussion arose later as to whether the discovery was not Borelli's, but all evidence shows that it was Malpighi who first saw this arrangement. Only in recent years has the completion of this discovery been brought about by one of our own number who showed the continuity of the muscle of the two ventricles in a double roll ending in the papillary muscles.[2]

Borelli was a man of marked genius but of irascible temperament, apparently also somewhat unscrupulous about questions of priority, but Malpighi was strongly attracted to him, and until they became estranged years afterward over a question as to the significance of respiration, regarded him almost as a father and constantly sought his counsel. In turn he was one of the few who would listen to Malpighi and approve of his iconoclastic doctrines.

After working thus happily for three years Malpighi, never in robust health and feeling the ill effects of the damp climate, left Pisa and returned to Bologna, having entered into the joys of anatomy and the philosophy of Galileo. While there he had projected a work with the aim of disclosing and remedying the evils of the medicine of that day, but this was not published and seems to have been destroyed in the fire which years later consumed his house.

In 1660 then he returned to Bologna and found Fracassati and Buonfigluoli there, with whom he resumed his studies. He became interested in the question of respiration and chiefly in the structure of the lung and the coursing of the blood through it, a process which had been shown by Harvey to take place, but which no one had as yet seen nor really comprehended. In two letters to Borelli in 1661 he describes what he has seen, urging his friend to see it too. He determined that the lung is not merely a porous mass into which blood is poured and again sucked out, but showed that the bronchi are continuous with the air vesicles and that the blood is constantly within the blood channels and never poured out into open spaces. One cannot do better than read the translation of these epistles which Sir Michael Foster prints in his interesting lecture on Malpighi, pp. 96-98:

"For while the heart is still beating two movements contrary in direction are observed in the vessels so that the circulation of the blood is clearly laid bare; and indeed the same may be even more happily recognized in the mesentery and in other larger veins contained in the abdomen. And thus by this impulse the blood is showered down in minute streams through the arteries after the fashion of a flood into the several cells, one or other conspicuous branch passing right through or leaving off there, and the blood thus repeatedly divided loses its red color and carried round in a sinuous manner is poured out on all sides until it approaches the walls and the angles and the absorbing branches of the veins.

"The power of the eye could not be carried further in the opened living animal; hence I might have believed that the blood itself escaped into an empty space and was gathered up again by a gaping vessel, and by the structure of the walls. But an objection to this view was afforded by the movement of the blood being tortuous and scattered in different directions and by its being united again in a determinate part. My doubt was changed into certainty by the dried lung of the frog which to a very marked extent had preserved the redness of the blood in very minute tracts (which were afterwards found to be vessels). Where, by the help of our more perfect glass, there met the eye no longer scattered points resembling the skin which is called sagrino but vessels joined together in a ring like fashion. And such is the wandering about of these vessels as they proceed on this side from the vein and on the other side from the artery that the vessels no longer maintain a straight direction but there appears a network made up of the continuations of the two vessels. This network not only occupies the whole area but extends to the walls and is attached to the outgoing vessel. Hence it was clear to the senses that the blood flowed always along tortuous vessels and was not poured into spaces, but was always contained within tubules and that its dispersion is due to the multiple winding of the vessels. Nor is it a new thing in nature to join to each other the terminal mouths of vessels since the same obtains in the intestine and other parts.

"All this you will see exceedingly well if you examine the turgid lung of a frog with a microscope of a single lens against the horizontal sun."

The significance of this discovery of the capillaries was of course enormous as it cleared up great difficulties not only in the explanation of the physiology of the circulatory system and respiration but especially in that of the glands, for now the function of the gland cells and the ducts could be rationally explained. As to the blood there still reigned obscurity. Malpighi, with the rest, thought the red color generally diffused, and even when several years later in his tract upon the omentum and adipose tissues he describes the corpuscles chiefly in their agglutinated condition as long rolls, he regards them as fat cells and compares them with red coral.[3]

As to respiration, Malpighi was not especially happy in his surmises, for while he rejected the view of Aristotle that respiration cooled the blood and thus kept it from coagulation—a view accepted by Descartes, Swammerdam, and even Boerhaave—he leaned to the theory of attrition, thinking the motion especially important in favoring fermentation in the blood. This was disproven by the Englishman Hooke, who opened the chest of a dog and while the heart was still beating punctured the lungs everywhere with minute holes. He then caused a blast of air to be blown through them and

[2] J. B. MacCallum, Johns Hopkins Hospital Reports, 1900, Vol. IX.

[3] Malpighi observed corpuscles in 1665; Leeuwenhoek described them in 1673; Swammerdam saw them in the frog in 1658, but his publication was in 1737.

thus, although the air leaked out of the holes he had made, the lungs were kept distended with fresh air and motionless and the dog lived for some time. An epistolary polemic between Borelli and Malpighi on the subject was probably the beginning of the rupture between them. Borelli proved that the air entered passively and that it did not entirely leave the lungs at each respiration and he had the luminous idea that the air itself was of use and that it contributed to the functions of the blood—a true divination. Incidentally Malpighi explained the frog's method of respiration which puzzled Borelli, showing that the frog practically swallows air so that respiration would be prevented by holding its mouth open—not, however, by opening its thorax.

Even at this time Malpighi was not exempt from violent attacks from his contemporaries who derided his teachings. One of his former students, Mini, who later became professor at the University of Bologna, attacked him in 1665 in a public denunciation of his teachings, and in 1678 wrote a book against him with the title "Medicus igne non cultro anatomicus," attempting to show the uselessness of anatomical studies in the cure of the sick as compared with a knowledge of the medicines which the fathers had found to be useful. Malpighi grew impatient and replied with some heat to this attack, as it is said, although I can find in his works no printed report of this reply. He must have been much comforted by the support of such men as Bartholin, Willis, and others whose opinions he knew he could respect.

In his earlier years Borelli had lived and taught in Messina and now the news came to him of the death of Pietro Castelli, who had held the chair of medicine. He immediately wrote to recommend his friend Malpighi as the most fitting successor, and the senate accepting his suggestion sent a polite letter to Malpighi requesting him to come there and teach the principles of medicine. This offer he accepted without much hesitation, and in 1662 we find him on his way via Naples to Messina. There in that most beautiful land, surrounded by the teeming Mediterranean he was in a naturalist's paradise. Every kind of animal and plant was at his service. Creatures of the sea were especially abundant and he availed himself of this profusion in marvelous fashion. Thus in the sharks he found the spiral intestinal valve and observed the viviparous habits of some forms. In the swordfish he saw that the optic stalk is composed of a twisted or folded plate, although he did not recognize the significance of this as showing it to be merely a crumpled diverticulum of the brain. He wrote at once to Borelli, who answers in a tone that seems quite modern:

"I was astounded by the drawings of the optic nerve of the swordfish, of which observations you should make great capital, and should easily find traces of this in other larger animals, such as the ox. If it prove to be so I should advise you to compose a treatise upon the subject and have it published."

It was in these fishes, too, that, without knowledge of Willis' book, he first attempted the investigation of the brain, a task so difficult, on account of the softness of the tissue which he could only overcome by the imperfect method of boiling the brain, that we can only feel surprised that he saw so much as he did. He discerned the cortical cells and their connection with the nerve fibers. Thus he appreciated the relation of the spinal cord and nerves to the brain, but unfortunately he regarded the nerve fibers as tubules (*budellini*) which carry a gross secretion from the nerve cells which he thought to have a glandular nature. This was really a Galenic idea and was soon afterward refuted, but Borelli believed it and quoted it in his book "*De motu animalium.*"

During this time Malpighi lived in the house of his interested patron Giacomo Ruffi, Visconti di Francavilla, who watched eagerly all his work and helped him in every way. It was then that he thought of writing a great work on anatomy, reviewing and criticizing all work already done and all views and theories already expressed in the light of his new discoveries. Haeser, in his history of medicine, regrets that this was never completed, but it seems now that we may feel grateful that when Malpighi consulted with Borelli and Fracassati about this, as was his wont, they wisely dissuaded him from thus examining the work of others, urging him to discover things for himself. Ruffi being of the same mind, he returned to his studies of the things themselves and nothing of the book remains except one or two chapters on the circulation and on the lungs which Atti has preserved.

During this time Malpighi's activity must have been enormous. It seems almost impossible that any one could have had time to make so many thorough studies in the intervals which elapsed between his enthusiastic epistles to Borelli and Fracassati and others by which it was his habit to announce each new discovery. His autobiography tells us, however, in the simplest concise way how he was occupied year by year.

"In the meanwhile dwelling in the country not far from the town in the villa of the illustrious Viscount Jacopo Ruffi I observed the structure of plants and there in the broken branch of a chestnut saw the air ducts or tracheæ which as I have learned exist also in other vegetables. I therefore wrote to Master Borelli about it, who answered me thus, 27 April, 1663:

"'I thank you for your description of your experience with the air tubes of plants which I have investigated too, but seeing them has not helped me further. Still I believe they are the same tubules that carry water and air and not different ones—as long as experience shall not demonstrate the contrary.'"

Evidently he made but little further study of plants at this time, for he goes on to relate how in his "horæ subsecivæ" he dissected fishes and other creatures, including various quadrupeds. It was then that he turned his attention to the tongue and its papillæ, which were of course well known, but thought to be secretory in nature. This he readily showed to be untrue by allowing the tongue to protrude and dry, when no secretion appeared from the papillæ. On the other hand he was able to show their provision of nerve filaments

and to deduce from this their gustatory function. Further he recognized the analogy between these and the papillæ of the skin, which he studied—one may say discovered. Particularly was he interested by the rete mucosum which he saw first of all and of which we speak in his honor as the Malpighian layer. There, as he pointed out, accumulates the pigment which makes the negro black. The nature of hair, feathers, and the external layers of the skin also fell under his inquiring search, although Leeuwenhoek perhaps described the epidermis more accurately in later years.

In 1665 he was violently attacked by one Michele Liparo, who upheld the ancient Galenic writings against the modern and published a book full of error and slander against Malpighi called *"Il Trionfo dei Galenici."* Malpighi, assuming the name of one of his students, Placidi di Papadopoli, answered him in an epistle *"Il Apologia dei Moderni,"* which Fracassati and Borelli wished him to publish, but which by his own will was not printed until the appearance of his posthumous works. This epistle, which begins with a harangue upon the ingratitude of mankind which neglects to read the great book of nature and leans upon authority, goes on to a great length discussing acutely the works of Galen and the interpretations put upon them by those who bow to his dictum.

It must have been during this time, although it is difficult to gather it from his autobiography, that Malpighi collected together his notes or made the new studies upon the viscera and their minute structure which forms the material for his book *"De Viscerum Structura Exercitatio Anatomica,"* which was printed in 1666 in Bologna. He writes: "The fourth year of my stay slipping by and the curriculum of lectures being completed I meditated a return to my own country. But it pleased the illustrious senate of Messina to request, on April, 1666, that I should continue yet another four years and with this in view I started to Bologna in the beginning of May with the plan, health, and my domestic affairs permitting, of returning in the autumn. In Naples I met the learned Cornelius and Leonardus and others of that school and talked and consulted with them as long as I was able, to the great recreation of my mind. In Rome it was my fortune to meet for the first time the famous Nicolao Stenone, who was very suave and friendly . . . and many others and at length reached Bologna safely. After a short bodily rest I had printed the material which I had arranged concerning the structure of the viscera."

This tract, printed separately at least once again by Petrum le Grand in Amsterdam in 1669 and finally in the various editions of his complete works, is one of great interest. It contains essays on the liver, the cerebral cortex, the kidneys, and the spleen, and each of these essays added much to what was known of the anatomy of these organs—indeed they shed the first clear light upon them. Malpighi apologized for writing of the liver after Glisson had written so well, but his contribution, notwithstanding that Glisson had written, is of great importance. He recognized the structure of the liver as that of a conglomerate gland, composed of hexagonal lobules, the number and structure of which he left to others to discern. He decided, too, that the bile-duct is the ordinary secretory outlet of the liver as in other glands their ducts, and that the bile is actually secreted by the liver and not by the gall-bladder. All these were important advances on the ideas that referred to the liver, chiefly the function of blood formation.

The essay on the kidneys is a masterpiece. Naturally he knew well the work of Lorenzo Bellini, who, in 1662, described the masses of tubules which make up the cortex, and began with this idea, soon discovering that the tubules are not straight but greatly twisted. He studied the form and general arrangement of the various tissues in the kidneys and we still hear his name in connection with the pyramids, although others must have known them before. He was the first to see the glomeruli, which also bear his name and which he correctly interprets as small tufts of vessels, for he could inject them either from the artery or from the vein. He describes them as hanging from the vessels like apples on a tree. The nature of their connection with the tubules was only explained clearly by Bowman much later, but Malpighi knew that they were connected and attempted to force colored fluids through them into the tubules but with no success. He also injected colored fluids into the ureter and in the living animal tied simultaneously the ureter and veins but without results of which he could be quite sure.

In the spleen he found "glands or vesicles distributed through the whole spleen like bunches of grapes. These have an oval form and are not much larger than the glands of the kidneys. They are, as I always observed, white, and even if the vessels are made turgid with a black injection, they preserve their color. They are soft and friable and one can see no cavity in them." He described also the vessels, parenchyma, trabeculæ (which he thought to be muscular), and the capsule and ligated the splenic artery in the dog without apparent effect.

To this there is appended a rather long description of the masses found in the heart after death and entitled *"De Polypo Cordis."* Evidently these were only postmortem clots, and even at the time Kerkringius, in his anatomical observations, contends that it is absurd to think that such masses were present in the living heart. Much more probable is it that they are produced in the dead by the cooling of the blood and the action of acids and other substances. The same mistake has recurred up to our own times and there is still alive a famous Anglo-Indian physician who has described, with vivid regret, the untimely death of many young soldiers and others from the development of such masses in the heart.

On his return to Bologna, despite his intention of going back to Messina in the autumn, he was persuaded to stay, and announced his intention to the senate at Messina, who, having already written to hurry him back, then answered accepting, though unwillingly, his resignation, which they took in very good part, wishing him every success and joy.

Thus he writes: "My domestic affairs being arranged and the house in Bologna settled, I went on with my studies with quiet eager mind." He practiced medicine, lectured, made autopsies with the aid of Fracassati and Buonfigluoli and earnestly sought the causes of disease. Besides these occupations he sought the society of friends and especially those of foreign cities, among whom were Sylvius de la Boe, Willis, and Bartholin, and tried by conversing with the celebrated men who passed through Bologna to advance his anatomy and to learn of remedies.

After this he turned his attention to the study of the lymph glands and of the uterus and its appendages. He was the first to describe the Gärtner's ducts as Gärtner himself stated in his description. This was not all, however, for he saw the uterine glands, studied the placenta which gave him difficulties, saw the Graafian follicles or ova and was the first to describe the corpora lutea. Again, he interests himself in the structure of bones, describing the flat bones especially noting that some bones contain no fat but blood—red marrow—such are the ribs, bones of infants, bones of birds, etc. He saw a cranium among the treasures of the Duke of Modena which was strangely thickened and curved with nodular projections, polished, and white like ivory. This skull he describes in the minutest detail as well as another in which he evidently had to do with a case of osteomyelitis of the jaw with sequestrum formation. Interesting, too, is his description of the aorta of the eminent Cardinal Bonacairsi, which was greatly dilated and lined throughout with bony plates and which he thinks might in time have become a continuous bony tube, as has already been observed in others. In another he describes the plaques as like drops of wax. These evidently contained no lime for they burnt readily into a black ash. He has also seen such plaques of bone in the meninges, and in the uterus and in the testicle has found stone-like masses, probably of the same nature. Thus, also, by the inspissation and precipitation of such materials he explains gout-stones. Next he is concerned with teeth and describes the teeth of a great variety of creatures, recognizing the different elements which compose them and describing the enamel as substantia filamentosa. About this time he tells us he became acquainted with Meibomius, Abraham Vilna, Joachim Elsner, and others.

Then, in 1667, he received a letter from Henry Oldenburg, the secretary of the British Royal Society, expressing their appreciation of his worth and asking him to correspond with them, to send them his works about plants, minerals, insects, particularly about the silk-worm, and to let them know of the works of other eminent writers in Sicily.

Malpighi answered with what he could of the unedited work of P. Costelli, Maurolicus, Borelli, and others, and set himself to work in 1668 at the cultivation and study of silkworms, "in which I tried to show not only the external mutations but the relations and structure of the viscera. This was a most tedious and laborious task, and fatigued by months of toil I was seized with a fever and an inflammation of my eyes in the autumn. Still, notwithstanding these difficulties, there was a mental delight in this work—in finding so many and puzzling miracles of nature that I cannot describe them with my pen. My collected observations, with drawings, I sent in the beginning of the year 1669 to the Royal Society."

In this dissertation he described what he saw in watching day by day the silk-worms which he hatched, and dissecting them at various stages. The minuteness and accuracy of his observations are astounding as he goes on to describe the external form, the musculature, the tracheæ, the nerves, heart, intestines, etc. Then the metamorphoses and the structures and habits of the adults. The generative organs and egg-laying occupy much of his attention, and all is set forth in the same clear, definite way. Particularly instructive are his references by way of comparison to other insects in which the structures differed slightly. The silk-spinning apparatus he describes and pictures in detail. Especially interesting, too, are his experiments with the tracheæ to prove their respiratory nature. If one apply oil so as to close them the animal dies. That this is not the poisonous property of that particular oil he shows by using other oils or even honey, relating that the creatures after any of these applications die in convulsions, while one may say a paternoster. When they are immersed in water and then allowed to dry they may recover when the water has dried off the orifices of the tracheæ. Much of his information on the silk-worm, including his observation that the eggs do not develop unless they have been mixed with the sperm of the male, was published later in his posthumous works in a letter to Buonfigluoli, etc.

We may here mention his work in connection with other insects, although much of it was not published until many years later. Cattaneo, who has written in an interesting way of Malpighi's studies of comparative anatomy, has collected together what he has written of insects. It was Malpighi who really discovered the tracheæ of insects and also the tubular heart which beats backward through the body, and about which Swammerdam disputed with him. The excretory tubules which hang about the intestine are his very own, too, and bear his name. He regarded them as hepatic in nature, although their real excretory character has since been shown. He drew with care the segmental muscles of the locust and of the pine caterpillar, and in a letter to Bellini in 1689 he actually describes their striation. The nervous cord, with its ganglia and pericœsophageal ring, the compound eyes and tactile antennæ—all these he described, and he even spent time on ascertaining the nature of the firefly's light, which he thought due to a sulphurous humor, since it gives a humid light which shines even under water. His crowning work on entomology, however, for which the studies of all these other insects were by way of preparation was the description of the silk-worm.

Even before the publication of this work was well under way he bought a villa nearby, at Corticella, and left his chair in Bologna to retire to the country and to study plants. Evi-

dently, however, this did not entirely preclude his indulging in the dissection of all sorts of animals. Everything that fell into his hands was dissected, even the creatures that came as food into his house were sacrificed first to his passion for dissecting, but as there was as yet no rational classification of animals his dissections were more or less isolated, for him at least, and he cannot be regarded as a founder of comparative anatomy except in the sense that he furnished an enormous material for others to analyze and correlate.

In 1669 Steno came to Bologna to visit him, and while he was there Malpighi showed him the muscles of the eye of a bird. Unfortunately it was not until after Steno had gone that he saw in the eye of a screech owl which he had opened laterally the inverted image on the retina—"trees, the house, —all inverted and whatever was at the right now came on the left."

Malpighi tells us in his autobiography that now having written of the structure and relations of the organs of animals he turned to the study of the anatomy of plants as being simpler and possibly capable of throwing light upon the other. Accordingly, after two or three years, he had published by the Royal Society the "Idea Anat. Plantarum," which was a sort of preliminary communication which expressed all the principles and the essential discoveries which he related in detail in his later work, the "Anatomes Plantarum." Curiously enough the "Idea Anatomes Plantarum," with its description of tracheid vessels, etc., was read at the Royal Society in 1671, just as Nehemiah Grew's work on the same subject appeared from the press. Grew described the tracheid vessels too and thus might claim the priority but he magnanimously resigned that to Malpighi, for he knew that he had made his observation in 1663.

For an idea as to the condition of botany at this time I may draw on Morini's interesting analysis of Malpighi's botanical work. Up to the time of Linnaeus and Tournefort the codex of botanists was the *Pinax theatri botanici,* the work of forty years of Gaspar Bauhin's life. It was the result of the feverish search of the Germans and Italians for the simples or plants described by Theophrastus, Dioscorides, Aristotle, and Pliny. Then, in the sixteenth century, there arose the botanical gardens; first in Padua, established by Bonafede and da Monte; then in Pisa, Bologna, and in 1577 in Leyden. No rational method of studying plants had been devised, however, until the time of Conrad Gesner, who knew them by their flowers and fruits and in this way gave the basis for the elaborate classification of Linnaeus. Cesalpinus was a botanist, too, as we see by his book (*De Plantis, libri* xvi, 1583), but they were yet in the beginnings of botany. Analogies, real or supposed, with animals dominated their ideas and the pith was regarded, therefore, as the seat of the vital principle, etc. Malpighi, too, clung for a long time to the idea that a circulation exists in plants comparable to that of animals and searched for valves in the conducting tubules. He had also the idea that there was a widely ramifying vessel taking food to all parts of the plant, and as he thought (having seen laticiferous and resin-bearing vessels) that he had surely seen this in some plants, hastened to apply the idea to all.

It would be impossible to enter into the details of Malpighi's enormous work which concerns especially phanerogams, but also some pteridophyta, fungi, galls, and parasitic plants. Hooke had seen plant cells and regarded them as merely cavities partitioned off from the general cavity. Malpighi, however, made a distinction between cells and fibers and vessels. With rare perspicacity he saw that all plants are composed of a complex of sacs or vesicles which constitute the fundamental tissues, and these he called otricoli. The generalization of this principle manifests the synthetic power of his mind. He had thus arrived at the modern distinction between parenchyma and prosenchyma, further than which he could scarcely go without a knowledge of protoplasm and the possibilities in the modification of cells.

His recognition of the continuity of leafstalks, branches, stem, and roots, and of the fact that the floral envelopes and cotyledons are modified leaves brought him very near to the ideas of Wolff and Goethe that all the diverse plant products may be traced from a few single types.

He described minutely with drawings of sections studied microscopically the wood and bark, the medullary rays, the tracheid vessels, scalariform and pitted vessels, sclerenchyma and woody fibers, the medulla, the nature of the annual rings, and so on, but erred in ascribing the origin of the wood fibers to the bast. From watching the growth of many plants he concluded that there was an essential difference between those which grew with one cotyledon only and those which started with two and thus divided as we now divide them, the phanerogamous plants. Not only this but he recognized that there is a fundamental difference in the arrangement of the fibrovascular bundles which corresponds with this division.

Most of his studies were, however, not merely morphological but sought to explain the physiology and laws of development of plants. Up to his time Cesalpinus had regarded the stamens as a means of draining the ovary and thought that the purified ovary could then produce seeds. Malpighi probably did not actually see the fertilization in the flower, for in studying the embryo he missed the micropyle which Grew had seen. Nevertheless, his work on the development of the ovum into the seed and of the ovary into the fruit and then of the germination of the seed is classical.

He recognized the need of air for plants, and again with his zoophysiological ideas ascribed the function of carrying the air to the tracheids. He found that on submerging them in water covered with a layer of oil they all putrefied and further that they died if he stripped them of leaves. Still he could never find the stomata of leaves and did not recognize the function of the chlorophyll, thinking that the gas exchange was equally carried out by the bark and the pith.

By ringing the stem of a plant he discovered the return current of elaborated materials from the leaves.

The sudden appearance of all this knowledge as to plants at a time when only the wildest speculations had resulted from what little thought had been expended upon them is another evidence of the great originality and independence of Malpighi's mind. His generalizations, too, from his various observations show the touch of genius which is missing in Grew's ponderous work. With the lower plants Malpighi concerned himself less. Rusts and smuts attracted his attention and he recognized the sporangia. In the mosses, too, he saw the sporogonia with the peristome and operculum and recognized the spore nature of the dust which one can shake out. Mucor and other moulds he studied too and saw their sporangia if not their spores. Apparently he was the first to describe the tubercles produced by nitrifying bacteria on the roots of leguminous plants, which have roused such interest in late years. Spontaneous generation was generally taught and believed in, but Malpighi took earth from a great depth, put it in a glass vessel which he covered with several layers of silk so that air and water but not the smallest seed could enter. Nothing grew. This seems a remarkable foreshadowing of Pasteur's work and we may imagine with what delight Malpighi would view a modern thermostat with its cultures of bacteria. Of infusoria or any microscopic plants he tells us nothing.

Although we have thus gone on to describe his botanical work at this point, it was not all the work of a year but lasted over several years, and while the *"Idea Anatomes Plantarum"* was published in 1671, the first part of the *"Anatome Plantarum"* appeared in 1675, and the second part, also published by the Royal Society, not before 1678.

In the meanwhile he was not neglectful of his anatomical interests and in an incredibly short time, amid his other occupations, he watched the hatching of hens' eggs, studying the developing chick at every interval by spreading it out on a glass slide and viewing it with his microscope, until in 1672, there was printed the book *"De Formatione Pulli in Ovo,"* which may perhaps be regarded as the cornerstone of embryology. This paper was sent to the Royal Society in February, 1672, but in October of the same year he finished another paper on the same subject, *"De Ovo Incubato,"* which enters much more fully into the details which he observed day by day in subsequent series of chicks. With his new method of floating off the embryo in water and spreading it on a slide, Malpighi was enabled to make many advances over his predecessors, of whom perhaps Harvey ought specially to be mentioned. Evidently, as he himself says, he entered into a very chaos when he undertook the study of this subject. Since he had no other method and seems not even to have dissected his embryos except in the latest stages but to have depended most largely upon their transparency, it is surprising to find how much he actually did see and draw in his figures. Hour by hour he described the changes which he could observe and later day by day. The accuracy and lack of error in his descriptions and drawings is quite marvelous, but it will be necessary to mention only the chief points. The formation and closure of the medullary groove, the primitive metameres, and the formation of the cerebral vesicles are clearly shown. Then the appearance of the optic vesicles with their stalk, the cleft in the vesicles, and later the lens formation are traced out. The twisting of the body and the appearance and development of the heart from a single bent tube to the perfect arrangement of auricles, ventricle, aortic arches, etc., are described, and the question arises in his mind as to whether the blood or the heart appears first. Later in his posthumous works he abandons this query as not worth labor. The division of the primitive portions of the brain is dwelt on and the modifications of each part described. With the later changes, owing, perhaps to the loss of transparency, he is less fortunate. There is a vague description of the liver, the clear white lungs, and the other organs. I can find no mention of the development of the intestine nor of the generative or renal apparatus. The appearance of the wings and legs and of the protuberances that later produce the feathers, and the feathers themselves are minutely followed. The breaking out of the egg, too, and the constriction and separation of the umbilical vesicles are as clearly described as in any modern book.

During this time he was attacked by many jealous enemies, even among those of his own faculty of Bologna, and so fiercely that Cardinal Pignatelli felt it his duty to interfere and protect him. Among these most prominent was J. Hieronymo Sbaragli, who, in an epistle "De Recentiorum Medicorum Studio, Dissertatio Epistolaris ad Amicum" (Göttingen, Sept., 1687), again, like Minus many years before, ridicules the studies of Malpighi, both anatomical, zootomical, and botanical, on account of their inutility in furthering the cure of disease. Of what use, he says, is the knowledge of the structure of the lung and the streaming of blood through it. Everybody knows that animals breathe but no one knows why, and it may be said even that in this modern seventeenth century, with all this new knowledge at our command, we are not even quite as successful in curing pneumonia as were the fathers of old. Everyone thought, until the work of Wirsung, that the pancreas was just a cushion to support the stomach. What better off are we to know that it has a duct? Above all of what use to cut up plants and study the hatching of eggs? Can one cure the troubles of women, knowing how the hatching of eggs goes on?

Malpighi replied somewhat querulously in a very long letter in which he republishes Sbaragli's epistle, then taking up clause by clause his objections. What difficulties must have met Malpighi in answering those taunts in those days when he could not persuade his readers of the future of his discoveries, even though he could see it himself, and how completely he has been justified. In our times the situation is different. Great good has been shown to come from some of these seemingly irrelevant discoveries and now everyone is willing to believe in such apparent side-paths of research and to wait hopefully for the practical result. Still Malpighi was not without a response. Precisely in the case of the

pancreas he recounts the knowledge of the day, saying that the secretion poured out from that duct, mixing with the bile and the chyle "provokes a peaceful fermentation," and that if it be prevented from so flowing or its character destroyed the person will waste away in an cachexia and that here at once we have a new knowledge of the cause of a disease. Of the hatching of the egg he immediately points to the hydatidiform mole and the abortions which are examples of the results of disturbance in this development. It was the fault of the times that such a ridicule could come to him—not the fault of his honest work.

The quarrel with the Sbaraglis, which lasted throughout Malpighi's life time and which concerned at first their adjoining estates and afterward, as we have seen, the doctrines of Malpighi, was marked by shameless acts of violence on the part of the Sbaraglis and even went so far that one of Sbaragli family was killed in an encounter with Malpighi's brother Bartolommeo.

It was about this time that he thought of collecting all his works and publishing a corrected edition. Then it was, too, that he wrote his autobiography which appears in his posthumous works and from which most of the details of his life have been learned. In this journal, which was by no means so detailed as his diary which he kept regularly from 1660 to 1694, he relates the main events of his life and discusses his works, criticising them and giving in full the criticisms of his contemporaries and his answers. He freely points out the weaknesses of his works and as freely acknowledges the good work of others.

In 1680 Malpighi sent his portrait, painted by Tobar in oil, to the Royal Society with a complimentary letter. They put it up carefully in a frame and Malpighi wrote to thank them for their care.

In 1683 he sent them a letter on the structure of the uterus, on a malformed kidney, on horns, glands, etc. The epidermal structures had long interested him and he devotes himself for a time to the study of hairs, feathers, and horns, studying the latter from their embryonic state in the bull and even describing a curious case in which a horn developed in the neck of one of these animals.

In the next year a fire broke out in his house, the villa at Corticella, and destroyed it completely together with many of his cherished possessions. A letter to Redi, which is published in his works (Opere de Fr. Redi, 1811), gives us an idea of the desolation into which he was plunged by this disaster: "I live, if it can be called life, in idleness, without other aim than to distract my grief. A chance fire in my house in the last month has burned what little I had, my notes in manuscript, the microscopes and lenses—only one was saved and a short time afterward this was stolen from me with a little money. I must recognize in this the voice of heaven, the more that to my old ills there are added articular pains which fetter me close so that nothing remains to me but to study and enjoy as best I can the work of others."

The correspondence with the Royal Society was interrupted from this time, 1684 until 1688, when they sent him a letter saying that they held him in high respect and asking for his most recent discoveries. He responded with the "*Epistola de Glandularum Conglobatarum Structura,*" in which he describes the distribution of these masses in various animals, their consistence, form, and color and their relation to the blood-vessels. He recognized, too, that they formed a portion of the lymphatic system and were directly intercalated in the lymph channels, although, as he tells us, these channels are so delicate and friable that it is practically impossible to dissect them out or even to obtain a very satisfactory injection. He names them lymphatic glands and goes on to describe some pathological changes, such as tuberculosis of the gland which can be recognized from his description, but which he also designates as tuberculosis, describing the relation of this lesion to the analogous condition in the lung.

Malpighi was now sixty years old, and after this there was hardly anything more of importance from his pen. It is true that he wrote, as we see in his posthumous works, notes upon flukes and tænias which he found in various animals, but they are not particularly happy descriptions. In the tænias he saw the suckers which he regarded as eyes with closed lids and the hooklets which he thought the teeth about the mouth; he could see no intestine, but the uterus with its eggs he saw, although he did not interpret it.

In 1691 he was asked by his old friend Cardinal Pignatelli, now Pope Innocent XII, to come to Rome to be his archiater or personal physician. Malpighi hesitated, partly on account of his ill health, partly because he had no taste for the position, but the pope would take no denial, and he set out for Rome. His autobiography tells us nothing of the period which followed this. He left Bologna, though, amid the general regret of the people who were loud in their expressions of affection and admiration, and reached Rome where he was received with profound respect. In 1693 Waller, the secretary of the Royal Society, wrote to congratulate him on his new position, and Malpighi answered, later writing to describe the earthquakes in Sicily. In July, 1694, he had an apopletic attack, the nature of which he recognized. It filled him with gloomy forebodings of his approaching end and he hurried to put in order his worldly affairs and to collect his notes—the notes which later appeared in his posthumous works. In November another attack came upon him as he had foreseen. On his deathbed he instructed de Fabri to send the rest of his manuscript to the Royal Society, and this wish was carried out by Buonfigluoli, his lifelong friend. They were properly printed by Churchill in 1696, and twenty copies were sent to Buonfigluoli. Malpighi died on November 29, 1694, in the Palazzo Quirinale. To Baglivi fell the dolorous task of performing an autopsy and embalming the body, which was afterward transported to Bologna and buried in the Church of San Giorgio. Baglivi's report is concise and I may repeat it here:

"Marcellus Malpighius ann. aetat 66. circiter, temperamenti ad siccum vergentis, mediocri corporis habitu, & mediocri pariter statura praeditus; cum per decursum plurium virilitatis suae annorum obnoxius fuisset vomitibus & secessi-

bus biliosis, & post horum suppressionem vomitibus acidis, palpitationibus cordis, calculis renum & vesicae, urinis cruentis, & interdum affectionibus podagricis levioribus: demum exacerbatis his omnibus post illius adventum Romam, praesertim palpitatione cordis, calculi renum, & sudoribus quibusdam vespertinis, iisque mordacissimis, correptus fuit apoplexia 25. Julii ann. 1694, hora circiter meridiana, praecedentibus curis, & animi passionibus, &c. Apoplexiae accessit paralysis totius dextri lateris corporis, tortura oris & oculi pariter dextri, &c. Die 29. mensis Novembris ejusdem anni denuo correptus fuit apoplexia post injectum consuetum clysterem hora matutina. Novam hanc apoplexiae invasionem praecesserunt gravissimae vertigines cum exacerbatione calculosa vesicae fere per integrum octiduum; inappertentiae, & reliqua symptomata antedicta graviora erant: sed vehementior his omnibus fuit novae apoplexiae insultus; nam irritis quibuslibet remediis post quatuor ad invasionae horas, migravit ad superos.

"Sectio Cadaveris.

"Secto cadavere observavi, sinistram pulmonum partem aliquatenus flaccescentum lividam, praesertim inposteriori illius parte, qua dorso adhaeret. Cor erat mole sua auctum, & praecipue parietes sinistri ventriculi, qui duorum digitorum latitudinem aequabant. Bilis in vesica fellea valde nigricabat: Ren sinister in naturali statu erat, dexter contra quasi medietate minor sinistro, ejusque pelvis adeo dilatata, ut duo digiti commode intrudi possent: ob hanc pelvis dilatationem succedebat, forsan ut calculi in renibus geniti statim in vesicam descenderent, & e vesica foras prosilirent, ut pluries mihi testatus est, dum esset in vivis Vir optimus. In vesica urinaria parvus calculus aderat, qui quatuor diebus ante invasionem ultimi accidentis apoplectici inibi descenderat, & descendendo vertigines illas ultimas exacerbavit. Reliqua viscera naturalia optime se habebant.

"Aperto capite, in cavitate dextri ventriculi cerebri duas libras circiter sanguinis nigri & grumosi extravasatas invenimus, quae sanguinis evasatio apoplexiae causa fuit & mortis. In sinistro ventriculo residebat aqua sub flava ad pondus sesquiunciae, eique intermixtae erant minimae arenulae exigua quantitate. Vasa cerebri sanguifera erant undequaque varicosa. Universa dura mater fortiter ac praeternaturaliter adhaerebat cranio."

Even more detailed and interesting is the account of the personal history of Malpighi which we find in the note of J. Marie Lancisi, which is printed in the Proceedings of the Royal Society and which I may repeat in full:

"The incomparable Malpighi who industriously applied himself to very serious Studies was of a good Habit of Body and had seen 66 Years, but he had frequent Sicknesses; Sharp Vomitings did torment him for 20 years. He was troubled with the gravel, a Hæmorrhagia in the Kidneys, a Rheumatism fluxious which with the troublesome consequences augmented his Infirmities. Scarce had these Evils given him some Respite when a cruel palpitation of the Heart with an unequal Pulse came upon him. Moreover 4 years before his death a sharp and biting sweat failed not all the summer to trouble him every night. Pope Innocent XII having called him to Rome to make him his chief Physician he began the first year to lose his fresh Color. In the second he voided many Stones without much pain and in the third which was the last of his life he found himself oppressed during the Winter with a difficulty of breathing.

"His health being thus insensibly undermined and a bilious looseness returning ever and anon he was at length seized with a Vertigo and loss of speech and Contorsion of the mouth (Spasmus Cynicus) and a palsy of half the right side, and tho there was appearance that he was out of danger by Bleedings, Purges, Diuretics, Antapoplectic medicines, yet one might see by his melancholy countenance but especially his want of memory that there was lodged in his Brain some melancholy Humour. Therefore perceiving his end drawing near, he signed with his Hand 3 days before his death his Posthumous works which he had ordered to be delivered to his Colleagues of the Royal Society at London. Then having confessed himself with great humility he attended generously with faith in God the death which appeared to him certain and not far off and on the 28th of November, 1694, a terrible apoplexy finished in the space of four hours this so precious life.

"The learned man foresaw that he should end his days by an Apoplexy and therefore forbad his friends to open his body until 30 hours after his death for he knew well enough that some who seemed dead on a sudden have revived some hours after. When he was opened we found the bladder of Gall abounded with a black Gall. The left kidney had nothing amiss but the right was twice as little and had its Pelvis twice as big which discovered the cause of the easy descent of the stones. We found in the bladder a little Stone that seemed to have fallen into it a few days before. The Lungs appeared withered with some mark of corruption on the back side. The Heart was bigger than ordinary, and the sides of the left ventricle felt harder and thicker in some places than in others. Yet there was no polypus found in it.

"The right ventricle of the Brain contained almost two ounces of extravasated blood and the left ventricle was swelled with a thick and yellow sort of Phlegm which weighed more than an ounce. Moreover the dura mater stuck closer to the skull than is usual. This proves that the conglobated glands in the whole body had thrown into the mass of the blood an acid lymph, and that the conglomerated glands of the hypochondria—especially those of the liver had thrown into it a melancholy humor and that these two sorts of humors being carried into the vessels of the Brain had disposed the blood to coagulate there, and that having there corroded and broken the tunicles which served for a stop to them they had run into the cavities where they caused death without a remedy.

"J. Marie Lancisi."

It is difficult for any one person to form a just estimate of

Malpighi's worth because his activities, like those of Virchow, ramify into so many widely different researches that there are few even at this day who can appreciate their details. Anatomy both human and comparative, physiology, general medicine, embryology, and botany—these, together with a minute study of entomology in both its anatomical and physiological aspect, were the things that occupied his mind. We cannot but regard his anatomical discoveries as of the first importance, and chief among these the capillary circulation and the explanation of the structure of the various viscera. His other numerous discoveries form a mass of new facts, such as it has been the fortune of scarce any anatomist to produce. Together, with his embryological studies, they form the basis for the great principle of the fundamental similarity among animals and the repetition of the principles of biology in the ontogenesis of various creatures.

In his botanical work he has always been compared with Grew, whose similar work on the same subject appeared at the same time. Sachs in his "Geschichte der Botanik," contrasts the two, pointing out that while Grew spent his whole life on phytotomy and amassed a quantity of facts, theorizing only too profusely on them, Malpighi tells us in a genial conversational style of his observations without undue surmises or philosophy.

After all is considered the most enduring things in Malpighi's books are his perfect honesty, his extraordinary keenness and good sense in the interpretation of what he saw and, his ingenious objective methods of observation. What he saw could not have failed of being seen very soon by others, but we are filled with wonder that quite alone, with his "quiet eager mind," he could have encompassed all, steadily searching out one thing after another throughout his forty years of restless activity.

TYPHOID APPENDICITIS WITHOUT OTHER INTESTINAL LESIONS.

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The recent study of the bacteriology of appendicitis has demonstrated the presence of a variety of micro-organisms in this condition. While it is not our purpose to enter into a lengthy discussion of the bacteriology of this disease, yet we shall briefly refer to the principal bacteria found in this process.

In "The Vermiform Appendix and its Diseases," by Kelly and Hurdon, the various organisms found in appendicitis are mentioned. The principal aërobic bacteria are *B. coli communis, Streptococcus pyogenes, Staphylococcus aureus, B. pyocyaneus, B. vulgaris, Pneumococcus, B. lactis aerogenes, B. alcaligenes,* various members of the hog cholera group, the *B. Friedländer* and the *B. pseudo-diphtheriæ.* It is not thought that all of these are the primary causes of appendicitis. Probably *B. coli, B. pyocyaneus,* and *Streptococcus pyogenes* are the most frequent causes of inflammation of the appendix. The *B. tuberculosis* and *Actinomyces hominis* produce special infections of the appendix.

Quite a number of anaërobic bacteria are mentioned by Lanz and Tavel [1] as occurring in appendicitis, but it is difficult to determine just what part they play in the actual production of the disease. Among the known pathogenic anaërobic bacteria they mention *B. aërogenes capsulatus* and the *B. edematis maligni.* Others mentioned are *B. pseudo-tetani,* and *B. ramosus, B. fusiformis,* and *B. furcosus.* These anaërobic bacteria may act as secondary invaders, producing principally gangrenous appendicitis. For an excellent account of this subject one should consult Kelly and Hurdon's book.

[1] Revue de Chirurgie, 1904, Vol. XXX, pp. 43-215.

Appendicitis and Typhoid Fever.

Although simple appendicitis and appendicitis with the characteristic lesions of intestinal typhoid both occur in this latter disease, as yet we have been unable to find any records of an uncomplicated primary appendicitis from which the typhoid bacillus has been isolated.

Hapfenhausen,[2] cited by Kelly and Hurdon, has investigated 748 cases of appendicitis, and in 36 of these cases there was a history of previous typhoid. The date of the typhoid ranged from two months to 40 years before the attack of appendicitis, and two other post-typhoid appendicitis cases are described by the above authors.

Routier [3] observed a case of appendicitis which terminated in an abscess, and which followed typhoid fever, and Anghel [4] reported an appendicitis following an attack of tonsillitis during typhoid fever. Dominici and Letulle [5] produced this disease in rabbits by injecting the typhoid bacillus into the ear vein, and Adrian [6] caused thrombi, hemorrhages, and necroses in the lymphoid follicles of the appendix in a similar manner. Mühsam,[7] by first crushing or bruising the appendix in rabbits, was able to produce inflammation of the appendix by injecting one cubic millimeter into the ear vein.

It will be seen from these clinical and experimental reports that appendicitis must often be associated with the typhoid

[2] Rev. de la Suisse Rom., 1899, tane 19, p. 105.
[3] Semaine med. No. 1, p. 6, 1897.
[4] Anghel, Thèse de Paris, 1897.
[5] Semaine med. No. 10, p. 73, 1899.
[6] Mitt. aus d. Grenzgebiet. d. Med. und Chir., B. VII, p. 736, 1901.
[7] Deutsche Zeitsch. f. Chir., Bd. 55, H. 12, p. 143, 1900.

bacillus. Our case, however, seems to be one of primary typhoid appendicitis, unassociated with any recent intestinal lesions, and as the typhoid bacillus was obtained from the lesions, we have thought it of interest as bearing upon the subject of typhoid infection and appendicitis.

Clinical History of Case.

The case which we wish to report was that of W. D. M., a medical student 24 years of age.

His previous history showed that he had a very severe attack of typhoid fever thirteen years before his present attack of appendicitis. Several other members of his family were attacked with typhoid at the same time, and all recovered.

On March 21, 1905, at 6.30 in the morning, he was attacked with a severe pain in the entire abdomen, which later became localized in the right iliac region. This was followed by nausea, vomiting, and slight diarrhœa. The patient had eaten freely of peanuts the night before. The temperature on admission was 100° F., but after the operation, which immediately followed, it never exceeded 99°.

An appendectomy was performed by Prof. I. R. Trimble at 5 o'clock p. m., and the patient made a complete and uneventful recovery.

Pathological Examination of Specimen.

The appendix on inspection was about three times the normal size, and about midway between the tip and the intestinal attachment the wall was thin and gangrenous, and about to rupture from distension. It was bent like the letter C.

The mucous membrane was covered in places with a dirty gray fibrinous membrane, and at its base there was an irregular ulcer. The lumen contained three soft, putty-like light-yellow concretions.

Histo-pathology.—On viewing the section under a very low power the mucous membrane and the submucous coat as well as the peritoneal layer are thickened and congested. A portion of the mucous membrane is still present, but at irregular intervals along the lumen of the appendix the mucous membrane has disappeared and is replaced by the thickened infiltrated submucous coat. The mucous membrane under a high power shows distinct exfoliation of the superficial epithelium. The intertubular tissue is thickened and contains numerous dilated capillaries and small arteries, many of the vessels show a collection of polymorphonuclear leucocytes in the plasma or outer zone of lumen and some leucocytes can be seen wandering through the walls of the vessels. The thickened intertubular tissue contains about an equal number of lymphocytes, proliferated endothelial cells, and polymorphonuclear leucocytes, and a few of the latter can be seen within the lumen of some of the mucous glands. The submucous coat is also richly infiltrated by groups of lymphocytes, proliferated endothelial cells, polymorphonuclear leucocytes, and a few plasma cells, and the solitary follicles seem increased in size, and the cellular infiltration of this coat proceeds from these thickened lymphatic structures. The muscular coat shows fatty degeneration and is also richly infiltrated with polymorphonuclear leucocytes and contains here and there small groups of pus cells mixed with lymphocytes. The arteries of the submucous and muscular coats all show a peripheral zone of leucocytes. The peritoneal coat presents a remarkable picture. It is greatly thickened and contains numerous distended capillaries and small arteries. The adventitia and perivascular lymph spaces of these vessels contain numerous lymphocytes and polymorphonuclear leucocytes. The wavy thickened tissue of the peritoneum is diffusely infiltrated by polymorphonuclear leucocytes, and it also shows numerous scattered areas of hemorrhage and in a few places some fibrin. The condition is not a peritoneal exudation but simply an infiltration of the thickened meshes of the peritoneal coat. In areas where the mucous membrane has become lost the thickened submucous coat is either covered by a thin layer of coagulative necrosis or consists simply of a raw suppurating mass of fibrin and pus cells. The submucous coat beneath these areas is tremendously thickened and seems to consist almost entirely of areas of hemorrhage and polymorphonuclear leucocytes and a few eosinophiles. The muscles beneath the thickened submucous coat are more richly infiltrated with pus cells. The peritoneum is thickened and contains more pus and fibrin.

In other sections taken from the appendix, there are no signs of distinct ulceration, and the glandular structure of the mucous membrane is fairly well preserved, but the proliferation of surface epithelium is very marked and the surface is covered in places by bile-stained masses of proliferated epithelium, lymphocytes, and a few pus cells. There are no distinct complete losses of mucous membrane as those noted above, and the condition of the various coats is similar to that described above. There is a curious condition of the lymphatics of the muscular coat present; these are greatly dilated and closely packed with small masses of lymphocytes.

The section made from the mesoappendix shows that the purulent infiltration has not extended to this tissue.

Bacterial Staining.—On staining the sections with eosin and methylene-blue the superficial areas of necrosis are seen to contain numerous bacilli of two distinct kinds. One variety is long and thin and probably represents the *B. pyocyaneus.* The other is small and ovoid and is probably the *B. typhosus.* A few bacilli can be seen in the purulent infiltration of the submucous coat, and the dilated lymph spaces of the submucous and muscular coats contain masses of the smaller bacilli, which are probably typhoid bacilli; the thickened peritoneum does not contain any bacilli, and it can thus be seen how these organisms, although gradually advancing toward the serous coat, have not yet penetrated this structure.

The lesions of the appendix, as clearly shown by the photomicrographs, represent a mixture of two distinct processes, if we follow out the classification found in Kelly and Hurdon's book.

The portion of the submucosa which forms the base of the ulcer, and even the muscular and peritoneal coats, corresponds to the condition called acute diffuse appendicitis. This variety

shows cloudy swelling of the surface epithelium, ulceration, and general infiltration of the coats by polymorphonuclear leucocytes. This process was probably caused by the *B. pyocyaneus.*

In other portions of the appendix, where there is no surface ulceration, a marked proliferation of the endothelium of the lymphatic spaces appears, and the polymorphonuclear leucocytes are not so numerous. These changes are more characteristic of typhoid fever, and are probably the reaction to the presence of the typhoid bacillus.

Description of Photomicrographs.

The photomicrographs show the lesions of acute diffuse appendicitis, together with the proliferative changes characteristic of typhoid infection of the intestine.

Fig. 1 shows a desquamation of the surface epithelium, and a proliferation of the cellular elements of the intertubular tissue and the submucous coat of the intestine at "a" and "b." At "b" under a high power the cellular exudate consists mainly of lymphocytes and proliferated endothelial cells.

Fig. 2 shows the thickened intertubular tissue under a high power, and a cross section of a mucous gland can be seen in the center of the picture. The tissue surrounding this gland consists mainly of small lymphocytes and endothelial cells. A few polymorphonuclear leucocytes are also present, and these can be occasionally seen wandering between the epithelial cells into the lumen of the gland.

Fig. 3 shows the infiltrated submucous coat at the edge of one of the ulcers, and consists almost entirely of proliferated endothelial cells and small lymphocytes, with small, round, darkly-staining nuclei. The first three photomicrographs are all taken from the edge of the ulcer near the surface and represent the proliferative changes described by Mallory in typhoid infection of the intestine.

Fig. 4 indicates in a striking manner the condition known as acute diffuse appendicitis. The lower half of the picture shows many groups of polymorphonuclear leucocytes separating bundles of involuntary muscle fibers, as indicated by the spindle-shaped nuclei. The upper half of the picture shows the greatly thickened peritoneal layer of the appendix. Several congested vessels are seen in the center of the picture, and the rest of the peritoneal layer consists almost entirely of polymorphonuclear leucocytes. Fig. 4 represents a reaction to *B. pyocyaneus.*

Bacteriological Examination.

Cultures were taken from the base and apex of the appendix, and two distinct varieties of colonies developed. One set of colonies was of a greenish color, and the surrounding agar was also green. The other set was moist and bluish to transmitted light. The moist colonies corresponded in their color and cultural characteristics to *B. pyocyaneus.* One cubic centimeter produced fatal purulent peritonitis in guinea-pigs. The second organ was found to be *B. typhosus,* giving all of the cultural characteristics of this organism.

The blood of the patient, in a dilution of one to fifty, was tested with the *B. pyocyaneus* and *B. typhosus* isolated from the appendix. *B. pyocyaneus* gave no reaction, but *B. typhosus* gave a positive reaction when mixed with the patient's blood.

This test was made one week after operation, and it seemed more likely that the reaction was produced by a recent infection with *B. typhosus* than by an attack of typhoid fever thirteen years before.

It is possible, however, that the typhoid bacillus may have remained in the gall-bladder ever since the attack of typhoid fever 13 years previous to the present attack.

Hunner[8] has reported a case of a greatly distended gall-bladder in a woman, aged 54, containing a thin, yellow pus. This was discovered after the removal of an ovarian cyst, and cultures gave a pure growth of the typhoid bacillus. Inquiry revealed the history of an attack of typhoid fever 18 years before the discovery of the typhoid bacillus in the gall-bladder.

This writer has also collected several other cases from literature in which the typhoid bacillus, usually accompanied by gall-stones, has been found in the gall-bladder at periods of six weeks (two cases), three and one-half months, and five months after attacks of typhoid fever. The most interesting cases are Miller's case occurring seven years after probable typhoid, and v. Dungern's case in which typhoid bacilli were found in the gall-bladder 14 years after an attack of typhoid fever.

Many of these cases showed cholecystitis, proving that complete immunity to the typhoid bacillus had disappeared. The typhoid bacillus, confined for years in the gall-bladder, may have found a more congenial atrium for infection in the normal lymphoid follicles of the appendix than that afforded by the scar tissue in the Peyer's patches of the small intestine.

The patient's blood also gave a positive reaction with a known typhoid bacillus, and the bacillus isolated from the appendix reacted with known typhoid blood from several different cases of typhoid fever.

The case is of interest for several reasons. The isolation of the typhoid bacillus and *B. pyocyaneus,* and the absence of *B. coli communis* in a case of acute appendicitis is the first point of interest; the second interesting feature is the production of the Widal reaction in a primary mixed typhoid infection apparently limited to the appendix.

We believe the infection was limited to the appendix, because 48 hours after its removal the temperature dropped to normal. The third point of interest is the presence of fecal concretions which resembled partly digested peanuts following the history that the patient had eaten many peanuts twenty hours before the attack.

The lesions found in the appendix were also of a mixed character. The diffuse purulent infiltration of the various coats was probably produced by *B. pyocyaneus,* while the proliferative changes in the intertubular tissue, and the submucous coat were the result of the typhoid bacillus.

[8] Johns Hopkins Hospital Bulletin, August-September, 1899, p. 163.

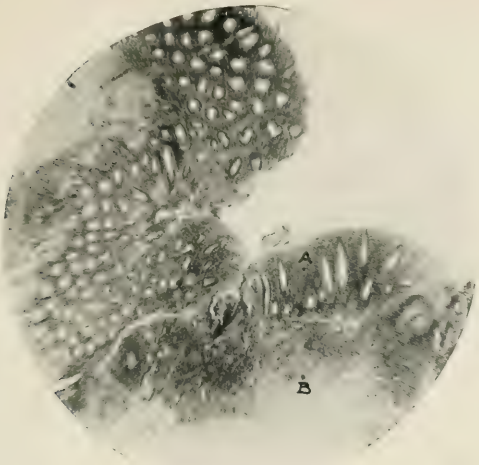


FIG. 1.—Mucous membrane on edge of ulcer showing loss of surface epithelium, infiltration of intertubular tissue at "a," and of submucous coat at "b."

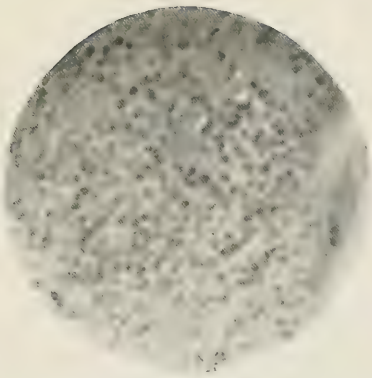


FIG. 3.—Submucous coat on edge of ulcer showing many proliferated endothelial cells and lymphocytes.

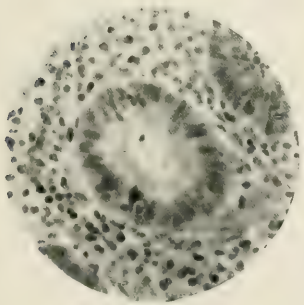


FIG. 2.—This shows a mucous gland of the appendix from Fig. 1 under the high power. The lumen of the gland contains a few polymorphonuclear leucocytes, and the intertubular tissue contains polymorphonuclear leucocytes, small lymphocytes, and endothelial cells.



FIG. 4.—Diffuse purulent appendicitis showing groups of polymorphonuclear leucocytes between the bundles of involuntary muscular fibers. The connective tissue of the peritoneum is also greatly distended by this purulent exudation which ends just before reaching the free surface of the peritoneal layer of the appendix.

THE PATHOLOGICAL ANATOMY OF EXOPHTHALMIC GOITRE.[1]

PRELIMINARY REPORT.

By W. G. MacCallum, M. D.,

Associate Professor of Pathology, Johns Hopkins University, Baltimore.

Notwithstanding the general agreement as to the histological characters of goitre in Graves' disease as described in literature, the most recent authors, A. Kocher and Reinbach, declare that there is no constant typical anatomical alteration. Nevertheless, in our series of 28 cases there has been found a lesion, similar to that described by Farner, with great constancy, although not always in the same degree. It is noteworthy that these cases were not derived from goitre regions. The more extreme alterations correspond exactly with those described by these various authors in the majority of their cases, but there are some in which these changes are found only in foci scattered through the gland.

Characteristic changes are to be observed in: (1) the form and size of the alveoli; (2) the character of the epithelial cells; (3) the character of the colloid; (4) the vascular supply; (5) the connective-tissue framework; (6) the lymphoid structures of the thyroid.

The alveoli vary greatly in size and form; many of them showing remarkable folding of the epithelium so that the cavities have the appearance of sending off long diverticula. Frequently these diverticula become constricted off from the remainder and new alveoli are thus formed. Sometimes these small new alveoli are very numerous and surround the older ones in the form of a colony which may be outlined by the denser stroma which surrounds the whole. This resembles almost exactly the alteration which was produced in the experiments of Dr. Halsted after the partial extirpation of the thyroid gland, that is, the condition of compensatory hypertrophy.

Changes in the epithelium consist in general in an alteration from the flat or cubical type to the high cylindrical form. The cells show frequent mitotic figures, and there are abundant granules of fat in their protoplasm. The cylindrical form is characteristic, but the height of the cells varies greatly. Alteration, such as the formation of the colloid cells of Langendorff and Hürthle and the *schmelzepithel* of Hürthle, are frequently found, but it seems probable that these are degenerative changes. Langendorff's canals are not to be seen. Occasionally there occur in the walls of the alveoli very large cells with very large vesicular nuclei which are intercalated in the lining of cylindrical cells. There appear also intercalated cells, or whole groups of cells, or even groups of alveoli lined with large, irregular cells provided with deeply staining nuclei and with granular eosinophile protoplasm. These have been described by Farner and Haemig. Their significance is not clear.

The alterations in the colloid consist chiefly in its marked diminution in amount and in the ragged appearance of that which is present. The colloid in some places is homogeneous in appearance and fills at least some of the alveoli, but in many cases it is reduced to minimum and appears only as a shreddy, vacuolated, granular mass. It is usually retracted from the epithelium, being connected with it by threads which run to the lines between the epithelial cells, and there is left a thin covering of colloid over the surface of the epithelium. It is apparently easy to show by the direct application of fixing re-agents to frozen sections of the thyroid that this separation from the epithelium is a retraction phenomenon and not due to the appearance of a colorless secretion over each cell. The colloid frequently contains desquamated cells and leucocytes. Its relations to the interstitial tissue and the lymphatic and blood-vessels have been much discussed. It has been pointed out by Quervain that it is impossible, with our present methods, to recognize colloid with certainty in the veins, that probably the hyaline material seen in the veins or in the lymphatics is largely composed of coagulated plasma, although it may contain a greater or less amount of colloid. We have found no particular excess of this hyaline material in the lymphatics in most of our cases.

The vascular supply is extraordinarily rich, the veins being especially large and distended with blood at the operation, although in the specimen as sent to the laboratory they are inconspicuous. The friability of their walls has been remarked upon by the operator. They lie embedded, for the most part, in the very abundant connective-tissue framework of the thyroid, which is in all cases quite definitely increased in density, considerable bands of fibrous tissue being found to run through the gland and to cause a distinct lobulation of the tissue. In this interstitial connective tissue there is found also a great deal of lymphoid tissue in the form of circumscribed, scattered, lymphoid nodules, with definite *keimcentra* and well defined architecture. Corresponding with this increase in the lymphoid nodules there is an enlargement of the neighboring cervical lymph glands and of the thymus.

The thyroids in many cases show the presence of circumscribed prominent nodules, sometimes in considerable number, which are composed of a more homogeneous tissue, and which on section are seen to be made up of uniform, small, round alveoli, usually widely separated from one another, and embedded in a hyaline connective tissue. These are lined with plump, rather cubical, epithelium, and may or may not con-

[1] Read before the Johns Hopkins Hospital Medical Society, May 15, 1905.

tain colloid material. They are usually very sharply marked out from the remaining thyroid and may sometimes show an excessive number of the altered epithelial cells described above, that is, those with giant nuclei and with eosinophile protoplasm. These circumscribed nodules are found in other conditions of the thyroid and are not characteristic of exophthalmic goitre. Cysts of various sizes usually containing a clear greenish, somewhat glutinous, fluid, may also occur.

No bacteria or characteristic cell inclusions could be demonstrated by microscopical, cultural, or inoculation methods.

The parathyroid glands were examined in nine cases and were found to be practically normal in all. They show in some instances a moderate atrophy of cells and induration or increase in the interstitial connective tissue, but the alterations do not seem to be constant nor sufficiently extensive to support the idea that the parathyroids have anything to do with the development of the disease known as exophthalmic goitre.

On the whole, the anatomical picture resembles most closely that produced by Dr. Halsted as a compensatory hypertrophy, and it seems probable that this may be explained by some previous injury to the gland, possibly from some foregoing infectious disease, such as influenza, etc., although a definite history of this kind cannot always be obtained. Similar changes may frequently be produced experimentally in dogs by the injection of some injurious material into the thyroid vessels, or even by the maintenance throughout a considerable time of a suppurative peritonitis in which, apparently by the diffusion of some poisonous substance, there occurs a destruction of many of the epithelial cells of the thyroid, which later are replaced by the compensatory hypertrophy of the remaining cells. The nature of the primary injury which may produce such a change in exophthalmic goitre is, however, by no means always clear.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

May 15, 1905.

Clinical Features of Thyroid Hypertrophy. Dr. Halsted.

Dr. Halsted said that one or more of the symptoms usually known as "exophthalmic goitre" might occur with various pathological conditions in the thyroid. Cysts, adenomata, carcinomata, and even "normal" thyroids had given such symptoms. No sharp line could, indeed, be drawn between perfectly normal people and those with extreme hypertrophy. The well-known symtom-complex is sometimes present without hypertrophy of the gland. The condition is more frequent in females (4.6 to 1) though late in life the proportion is smaller. The prognosis is bad and it is doubtful if complete recovery has ever occurred. Twenty-five per cent of all the patients die within a short time and the rest remain in a state of labile equilibrium. Acute cases occur—one, reported in Nothnagel, appeared in two days and disappeared in eight. The mild form of the disease has been particularly studied by the French; and all observers have noticed that there is no sharp line of demarcation between normal patients and those with mild goitre. In the cystic cases there has usually been no hypertrophy of the non-cystic portions of the thyroid. In the Johns Hopkins Hospital there have been 46 cases of goitre with symptoms operated upon. The majority of these were mild but a few were severe. There was one death in the series. And in this case nearly three-fourths of the gland was removed. At present non-operative treatment is being tried, and the X-ray is being used instead. The influence of this agent has been marked in certain of the reported cases but it is not prompt.

The Pathological Anatomy of Exophthalmic Goitre. Dr. MacCallum.

(See this Bulletin, p. 287.)

June 5, 1905.

Bacteriological Observations in Some Cases of Bronchiectasis. Dr. Boggs.

The application of Kitasato's method to the culture of organisms other than the tubercle bacillus was described, and also the special media necessary for cultivating *B. influenzæ*.

The bacteriological findings in five cases of bronchiectasis were then presented. Of two fatal cases, one rather acute in its course, with fever, night-sweats, and hemoptysis, and one of several years' standing, the first yielded an absolutely pure culture of *B. influenzæ* from the sputum and from the lungs at autopsy. Sections showed the organisms deep in the bronchial walls. The second showed an overwhelming preponderance of influenza bacilli, with a few colonies of pneumococcus. No cultures were obtained at autopsy. Sections showed the influenza bacilli deep in the bronchial walls and mostly intracellular.

The other cases were of a chronic nature, all with definitely demonstrable cavity formation, characteristic profuse sputum, and a history of exacerbations with fever and night-sweats. Of these, one has had profuse and repeated pulmonary hemorrhages during the past twelve years. This case gave pure cultures of influenza bacilli. One, clinically indistinguishable from the others, gave a great preponderance of pneumococcus on culture, with a few influenza bacilli, the same results being obtained from this case at an operation for drainage of the cavities. From this case also was obtained a micrococcus growing only on hemoglobin-containing media and producing on such media the characteristic sickening fetor of bronchiectatic sputa. The organism did not stain by Gram's method and grew but poorly after the first two generations, being lost on the sixth transfer. The remaining case yielded *B. influenzæ* in pure culture.

The principal points of interest deduced were: The close resemblance of these cases to chronic pulmonary tuberculosis, though in no case could tubercle bacilli or tubercles be demonstrated in the sputum or at autopsy. Their importance as possible sources of influenzal infections during inter-epidemic periods. The desirability of further bacteriological study of our chronic pulmonary diseases, and the impropriety of making an absolute diagnosis of tuberculosis when no tubercle bacilli have ever been found.

Acute Pericarditis in Pneumonia. DR. CHATARD.

(To appear in a future number of the Bulletin.)

A Study of the Physiological and Toxicological Actions of the Toxic Agent of Pneumonia. Therapeutic Observations and Indications. DR. BREM.

(To appear in a future number of the Bulletin.)

NOTES ON NEW BOOKS.

The Naked-Eye Anatomy of the Human Teeth. By THOMAS E. CONSTANT, L. R. C. P. London, and M. R. C. S. Eng. (*Bristol: John Wright & Co.: London: Simpkin, Marshall, Hamilton, Kent & Co., Ltd., 1905.*)

The title above is somewhat misleading. The book not only treats of the human teeth, but also of the mouth, the bony framework of the jaws, the muscular covering, the tongue, soft palate and tonsils, the salivary glands, the blood vessels and nerves, and the movements of the mandible. The descriptions are clear and the discussions of the questions which arise are thorough and most interesting. A good example is the chapter describing the movements of the lower jaw. The author shows that the temperomandibular articulation is not a simple hinge-joint and that the structures which form it are not kept in close apposition by the ligaments of the joint, which have little or no restraining power, except in preventing excessive movement. Apposition is maintained by the tonic action of the muscles that elevate the mandible and exercise a suspensory action upon it. The "dropping of the jaw" at the moment of death indicates the destruction of the tonicity of these muscles. He argues further that a hinge movement in the condyle during depression of the mandible is impossible and that the movement of the condyle is in reality a sliding one.

Such painstaking analytical studies of special anatomical regions are most valuable and must lead to important practical results. The book is to be recommended not alone to students of dentistry, but to all students of anatomy. It is well illustrated and excellently printed. It also has a good index.

Wharton and Stillé's Medical Jurisprudence. Vol. II. Poisons. By ROBERT AMORY, A. M., M. D., and ROBERT L. EMERSON, A. B., M. D. Fifth Edition. (*Rochester, N. Y.: The Lawyers' Co-operative Publishing Company, 1905.*)

It is manifestly impossible to review this work in detail, owing to the great variety of its contents. The present edition has been thoroughly recast and practically rewritten. Much of the material in former editions has been cut out and new matter more in harmony with present chemical and toxicological views has supplied its place.

We notice a full account of sulphonal poisoning, also of the evil effects of acetanilid and other coal tar preparations. Wood alcohol, too, is considered and the injury which ensues to the life, or at least to the vision of those who have been poisoned by it, is mentioned. Ptomain and toxalbumen poisons are also considered at considerable length. The possibility of death by tetany being mistaken for strychnia poisoning is not mentioned, although tetanus is considered. In some severe forms of general tetany the cramp-like character of the convulsive seizures might easily be mistaken for strychnia poisoning. It is gratifying to notice that the authors have evidently familiarized themselves thoroughly with the most recent literature regarding the newer poisons and have thus given us a book which will prove a safe guide to both physicians and lawyers.

The arrangement of the book may be somewhat criticised. There seems no good reason why the material contained in the appendix should not have been included under its proper heading in the main volume, or at least in footnotes explanatory of the text. The volume is a storehouse of valuable knowledge.

The American Year Book of Medicine and Surgery. Being a Yearly Digest of Scientific Progress and Authoritative Opinion in All Branches of Medicine and Surgery, drawn from Journals, Monographs, and Text-books of the Leading American and Foreign Authors and Investigators. Under the general editorial charge of GEORGE M. GOULD, M. D. Surgery. (*Philadelphia and London: W. B. Saunders & Company, 1905.*)

The value of this excellent Year-book has been fully tested by all who have consulted the previous issues of the series. The volume contains the newest facts in surgery and the latest developments and improvements in surgical practice. In the volume under consideration, for example, we find the latest observations upon the various methods of sterilization of the hands, a discussion of the merits of rubber gloves as compared with the use of Murphy's adhesive rubber dam, a resumé of Kraske's objections to the indiscriminate employment of the Trendelenburg posture in abdominal operations, a full discussion of the treatment of carcinomata and sarcomata by surgical operations or Röntgen-rays, observations on both local and general anæsthesia and the newer agents for securing them, a discussion of surgical intervention in diseases of the stomach in apendicitis, cholecystitis, etc. The extent and variety of the contents of this book in fact are somewhat bewildering and suggest the need of greater limitation in the number of topics and more condensation in their treatment if the present single volume is to remain one which can be easily consulted. The editorial work has been well done and the book as a whole is most creditable.

Clinical Lectures on Mental Diseases. By T. S. CLOUSTON, M. D., Edin. F. R. C. P. E., President of the Royal College of Physicians, Edinburgh; Physician-Superintendent of the Royal Edinburgh Asylum for the Insane, etc. Sixth edition. (*Philadelphia and New York: Lea Brothers & Co., 1904.*)

This new edition of a well-known and deservedly popular textbook represents many changes in scientific views. Probably no better index could be given of the present activity in the study of mental diseases than the modifications which have been made in this as compared with previous editions. The style is conversational and frequently displays the freedom and latitude of expression of the popular lecture. It is always interesting and suggestive. Rarely if ever has a more practical treatise on the treatment of insanity made its appearance. The author's classification of insanity, like everything else in the book, is a decided assistance to the student both in treatment and prognosis. In the headings of the chapter he uses alternative words which help the meaning materially; thus, for example, successive chapters are headed: "States of Mental Depression—Melancholia (Psychalgia)," "States of Mental Exaltation—Mania (Psyclampsia)," "States of Alternation, Periodicity, Remission, and Relapse (Folie Circulaire, Psychorythm, Folie à Double Forme, Circular Insanity, Periodic Mania, Recurrent Mania, Katatonia)," "States of Fixed and Lim-

ited Delusion (Monomania, Mono-Psychosis, Paranoia)," "States of Mental Enfeeblement (Dementia, Amentia, Psycho-Paresis, Dementia Precox, Congenital Imbecility, Idiocy)," "States of Mental Stupor (Acute Dementia, Primary Dementia, Dementia Attonita, Psychoma)," "States of Defective Mental Inhibition," etc. In the discussion of special topics as the distinction between melancholy and melancholia he is extremely lucid and judicious. He says: "Mere melancholy might be defined as a sense of ill-being and a feeling of mental pain with no real perversion of the normal reasoning power, no morbid loss of self-control, no uncontrollable impulses towards suicide, the power of working not being destroyed, and the ordinary interests of life only lessened, not abolished.

"Melancholia might be defined as mental pain, emotional depression, and sense of ill-being, usually more intense than in melancholy, with loss of self-control, or insane delusions, or uncontrollable impulses towards suicide, with no proper capacity left to follow ordinary avocations, with most of the ordinary interests of life destroyed, and commonly with marked bodily symptoms." Could the distinction be made any clearer?

We are gratified to notice that although, like other Englishmen, he still "shies" at the word Paranoia, and prefers some other title for fixed and systematized delusions, he is willing to print the hated name and to describe the condition to which it has been applied.

The ætiological classification of Skae in a modified form is retained and under the various headings many interesting clinical reports are given. Whatever may be said as to the scientific accuracy of such an ætiological classification (and much may with justice be urged against it) it is undeniable that this scheme of classification, if it can be arrived at with any degree of accuracy and fidelity to the symptoms present, is of great service in prognosis and treatment. The final chapter in the book, entitled, "A Summary of the General Treatment and Management of Insanity looked at as a whole: and on the Use of Hypnotics, Sedatives, and Motor Depressants," is most useful and should be in the hands of every practitioner who may be called upon to see insanity cases. In the present age of therapeutic nihilism it is gratifying to find an author who believes that certain remedies are indicated in specified conditions and is able to point out what are the best. The book as a whole will be most useful.

Essentials of Bacteriology. Being a Concise and Systematic Introduction to the Study of Micro-organisms. By M. V. Ball, M. D. Fifth edition, thoroughly revised by Karl M. Nagel, M. D. With 96 illustrations and 6 plates. (*Philadelphia, New York, London: 1904.*)

This compend gives evidence of careful work on the part of both author and editor, but it is apparent that the effect of extreme condensation has been to deprive it of any value except as an aid to students who are preparing for examinations. It could not be used as a laboratory manual, nor is it full enough to be of much service to one who did not possess a previous knowledge of bacteriology.

A Text-Book of the Practice of Medicine. By H. A. Hare, M.D., B. Sc. (*Philadelphia and New York: Lea Bros. & Co., 1905.*)

The author of this new candidate for honors in the field of text-books of medicine is well known for his works on diagnosis and treatment. Accordingly, the reader looks with interest to see how he has succeeded in this new venture. It is, of course, quite impossible to review a text-book in any great detail and one usually picks out certain points. Among these the treatment of lobar pneumonia is always interesting. As might have been expected, Dr. Hare's manner of handling this subject seems excellent. He emphasizes here as throughout his work the foolishness of using routine treatment and of giving drugs without definite indications for their use. The mistakes of giving anti-pyretic drugs, of beginning stimulation too early, and of the use of expectorants during the fever, are especially noted. In the discussion of the treatment of pleurisy with effusion, we think Dr. Hare might have laid very much more stress on the value of early tapping. The advisability of this seems to be definitely established, and to wait until there are signs of pressure or the fluid remains unabsorbed for a considerable time is hardly giving the patient the best chance.

The section on the diseases of the circulation is well written. It is interesting to note that in the discussion of the use of digitalis Dr. Hare states his opinion that digitalis through its abuse does almost as much harm as it does good. Attention is drawn to the necessity of carefully examining the state of the vessels before digitalis is given, and to the necessity of reducing arterial pressure, if that be high. This is a most important point and one which is frequently overlooked.

The section on diseases of the nervous system must be always more or less of a worry to the writer of a text-book of medicine. The question of classification is always a difficult one, and Dr. Hare seems to have done well in making this as simple as possible; to the student elaborate classification is always difficult.

We consider this a very satisfactory work. The descriptions throughout are clear and no space is wasted on unnecessary discussion. The sections on treatment are especially good. The publishers have done their work well and there are a number of excellent illustrations.

Diseases of the Heart. By Edmund Henry Colbeck, M. D., F. R. C. P. (London). Second edition. (*Chicago: W. T. Keener & Co., 1905.*)

This work, which is now in its second edition, deals especially with the clinical side of cardiac disease. The work is of medium size and this compelled the exclusion of many doubtful points, which is perhaps an advantage to the student and young practitioner.

The book opens with a section on the anatomy and physiology of the heart, after which the methods of diagnosis are discussed. One point of interest may be noted, namely, the explanation given of the visible pulsation so common in the third left interspace. The opinion is given that it may be due to enlargement of the left auricle, but is probably more commonly from the infundibulum of the right ventricle. The weight of opinion now inclines to the latter being the cause in the vast majority of cases. Under the discussion of blood pressure very little is said and no mention is made of what is probably the best instrument for ordinary clinical work, namely, the Riva-Rocci instrument. Dr. Colbeck might well have given greater space to this important subject.

Then follows the bulk of the work, namely, organic affections. The discussion of these is, as a rule, satisfactory, but it seems to us that the importance of arteriosclerosis is not recognized. Arteriosclerosis is not even found mentioned in the index. The lack of consideration given to this important subject seems rather surprising. The treatment advised seems very rational. It is somewhat unexpected to find that alcohol is advised as a cardiac stimulant and in comparatively large amounts. The administration of spirits up to ten or twelve ounces in twenty-four hours would seem likely to do harm, although smaller amounts might be useful. It is equally surprising to find so much doubt expressed of the value of digitalis in aortic insufficiency.

We quite fail to understand why Stokes-Adams disease should be placed under the heading of functional disorders. Altogether, we question the advisability of using such a book as this in preference to the excellent, more elaborate treatises which we have.

A Text-Book of Medical Chemistry and Toxicology. By JAMES W. HOLLAND, A. M., M. D., Professor of Medical Chemistry and Toxicology, and Dean, Jefferson Medical College, Philadelphia. (*Philadelphia and London: W. B. Saunders & Company, 1905.*)

This text-book is evidently intended for medical students whose training in physics and chemistry has been entirely insufficient to begin the study of medicine. The greater part of the book is taken up with elementary physics and organic and inorganic chemistry. Under the various substances toxicological considerations are included. At the end of the part on organic chemistry the alkaloids (p. 13), the ptomaines and toxines (p. 5), the proteids (p. 8), and the enzymes (p. 4) are included. The last division of the book is called "Physiologic and Clinical Chemistry," and under this head are discussed digestion, blood, milk, and urine. It is clear from the above that the author has attempted to touch upon too many subjects in this small text-book, with the unavoidable result that no part is very satisfactory. The fact that only twelve pages are devoted to the proteids and enzymes (and these might have been omitted without loss) would lead one to question the propriety of calling this a text-book of "Medical Chemistry." The day of the shot-gun text-book along these lines belongs to the past. A. S. L.

A Nurse's Guide for the Operating Room. Second edition, enlarged and revised. By NICHOLAS SENN, M. D., Ph. D., LL. D., C. M., Professor of Surgery, etc. Published under the direction of the Sisters of Charity, St. Joseph's Hospital, Chicago. (*Chicago: W. T. Keener & Co., 1905.*)

The previous edition of this Guide was reviewed in Vol. XIV of the BULLETIN. In the present edition additions have been made both to the text and the illustrations. We are gratified to find the author recommending the use of rubber gloves, an omission in the first edition. The directions given for the preparation of medicated gauzes, the sterilization of catgut, the preparation of drains, and the manufacture of the different antiseptic solutions are excellent. The most valuable portion of the book to many nurses will be the careful lists of instruments given as a guide to those who may be called upon to prepare for any desired operation, the lists of ligatures and sutures required, and the materials needed for the after-dressing. The illustrations of apparatus and instruments are numerous and generally well executed. "Important test questions" at the close of the book might have been omitted without any disadvantage to the work.

The Open-Air Treatment of Pulmonary Tuberculosis. By F. W. BURTON-FANNING, M. D., Cantab., Physician to the Norfolk and Norwich Hospital. (*London, Paris, New York, and Melbourne: Cassell & Company, Limited; Chicago: W. T. Keener & Co., 1905.*)

This little book of 172 pages, "intended to serve as a practical guide to the modern method of managing pulmonary tuberculosis," accomplishes the author's aim admirably, being a simple, concise, and straightforward account of our present attitude in the treatment of this disease; "based upon experience," the author writes, and indeed there is not a single paragraph which does not bear the mark of having come from one who has traversed the ground personally and thoroughly. The book is very readable, all but an occasional reference to the literature and to statistics having wisely been omitted. Following the introduction is a very short chapter on the etiology of pulmonary tuberculosis, a chapter which does not add materially to the value of the book, and in which the chief views on the source and method of infection, at present so uncertain and so warmly disputed, are treated briefly and with justice. Everyone appreciates that the most important thing in successful treatment is an early diagnosis. This point is well emphasized and the essential factors are considered. Many will criticise that the use of tuberculin as an aid in early diagnosis is only casually referred to in a paragraph of ten lines. The author states that he has no personal knowledge of its value for this purpose and that the profession in England as a body has shown some hesitation in adopting it on the ground that it is not altogether devoid of risk. Certainly in America it is used more commonly and esteemed highly, and the prevailing opinion is that with due care the risks are slight. What is said of the prognosis in the various types and stages of the disease and the necessity of selecting the proper cases for sanatorium treatment is scarcely less important. He says very judiciously that we must recognize how very insufficient even our best means are to fight the disease; we must be candid with the patient and must not promise too much, or "at the end of some months spent in treatment, the patient, whose malady perhaps never admitted of complete recovery, is apt to complain that he only embarked on the course under the impression that he would certainly be cured by so many months in a sanitarium. The false statement recoils on the head of the practitioner, and the treatment is discredited in the eyes of the laity." What is particularly gratifying is to note only here and there a reference to drugs, and even then with but little praise, and to read that "the well-known mixture of soda, tinct. nux vomica, tinct. gentian, and aqua chloroformi is prescribed, perhaps, more frequently in pulmonary tuberculosis than any other medicine." Everyone who has to treat cases of pulmonary tuberculosis and has not had the advantage of studying personally modern sanitarium methods, should read the book. He will certainly learn to avoid in the early stages the false security of creosote and cod liver oil and the laxity of telling patients to live in the open air and to eat plenty of food, with the feeling that by such advice the physician discharges his duty. "Precision," as the author says, "is the secret of success."

Outlines of Physiological Chemistry. By S. P. BEEBE, Ph. D., and B. H. BUXTON, M. D. (*New York: The Macmillan Company; London: Macmillan and Company, Ltd., 1904.*)

This book represents an effort on the part of its authors to deal with chemical questions which bear directly upon physiological problems. It is not intended as a laboratory guide. It deals with theories of the newer chemistry in a very elementary fashion and will be mainly useful to those persons who have been familiar with the older chemical views and desire to acquire a knowledge of the newer. To such persons it may be commended as giving an introduction to the subject.

Medical Philology. Gathered by L. M. GRIFFITHS, M. R. C. S. Eng. Part 1: A-El. (*Bristol: J. W. Arrowsmith, Quay St., 1905.*)

In this book of 100 pages Dr. Griffiths has afforded to the reader delightful glimpses of the original meaning of many words in common use and has corrected many misconceptions which have followed a false philology. Who would have thought, for example, that hangnail originally had nothing to do with the nails, but was simply "a corne or agnele in the feet or toes"? or that the use of the word bunion was formerly not confined to a disease of the foot but signified any kind of a bump or round swelling from violence, even upon the head? Or that jaw-bone was originally chawe bone? Or that chin-cough (whooping-cough) was originally kirk-cough, from kirk (to gasp)? There are many other curious examples of word changes which cannot well be referred to for lack of space. Every physician who has leisure for studies of this character should procure and read it. It is to be hoped that the accomplished author may find time and opportunity to continue similar notes through the remainder of the alphabet.

Acute Contagious Diseases. By WILLIAM M. WELCH, M. D., of the Municipal Hospital, Philadelphia, and JAS. F. SCHAMBERG, A. B., M. D., of the Philadelphia Polyclinic. Illustrated with 119 engravings and 61 full-page plates. (*Philadelphia and New York: Lea Brothers & Co., 1905.*)

This book deals with Small Pox, Chicken Pox, Scarlet Fever, Measles, Rubella (German Measles), Typhus Fever, Diphtheria, and their allied subjects, Vaccination, Variolous Diseases of Lower Animals, the Serum Treatment of Diphtheria, and Disinfection. The purpose of the authors has been to treat of those diseases which by their extreme degree of contagiousness require to be treated in a municipal hospital. The most complete and probably the most useful portion of the book relates to Vaccination and Small Pox. Here Dr. Welch's experience for thirty or more years is fully and instructively given. The history of vaccination which precedes the consideration of small pox is also well told. We do not remember at any time to have seen the fact so well brought out that the immunity which vaccination brings is due to the gradual attenuation of the original small pox virus by passing it through a series of inoculations in an animal which is not very susceptible to the disease.

As to the treatment of small pox by local applications to prevent permanent scarring, the authors are somewhat pessimistic and agree with Gregory when he said: "There is no peculiar method which can be devised for the prevention of pits and scars. The masks and ointments formerly in use for that purpose and so highly vaunted are in reality more hurtful than beneficial." The remedy which has proven the most useful has been tincture of iodine. The iodine treatment causes the postules to shrink and destroys the offensive odor." The use of the continuous warm bath is recommended in very severe cases of the disease. The use of red-light after the manner of Finsen in the experience of the authors has proven absolutely negative.

The section of the volume which seems next in importance is that which treats of diphtheria. The general treatment of the disease is not neglected, but, as might have been predicted, in the judgment of the authors the early use of diphtheria anti-toxin offers the best hope of curing the disease.

The other sections, while presenting nothing especially new, have been written with care and will prove of great value to physicians who consult them for instructions as to the best form of treatment to adopt in emergencies which may arise in the course of these contagious diseases.

The volume is exceptionally well illustrated and attractively printed. The text, it is stated, is based upon the study of 9000 cases of small pox, 9000 cases of scarlet fever, and 10,000 cases of diphtheria. Rarely have authors had access to such a mass of clinical material!

Progressive Medicine. A quarterly digest of advances, discoveries, and improvements in the medical and surgical sciences. Edited by HOBART A. HART, M. D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College, Philadelphia, etc. Assisted by H. R. M. LANDIS, M. D., Demonstrator of Clinical Medicine in the Jefferson Medical College, etc. Volume I, March, 1905. (*Philadelphia and New York: Lea Brothers & Co.*)

Among publications of its kind Progressive Medicine occupies a deservedly high place. It consists of careful abstracts and summaries of the literature for the period considered, with conservative criticism of advances made and proposed.

The present volume contains reviews in "Surgery of the Head, Neck, and Thorax," by Charles H. Frazier; "Infectious Diseases, including Acute Rheumatism, Croupous Pneumonia, and Influenza," by Robert B. Preble; "Diseases of Children," by Floyd M Crandal; "Laryngology and Rhinology," by Charles P. Grayson; "Otology," by Robert L. Randolph.

In each of these, the subjects for discussion have been well selected and the literature, both foreign and of this country, has been considered with sufficient detail to make the volume of practical value to the reader, as well as a good index to the best literature on the subjects.

Introduction à l'Etude Clinique et à la Pratique des Accouchements. Par LE PROF. FARAKENF et LE DOC. VARNIER. (*Paris: Georges Steinheil, Editeur, 1904.*)

A book so well known as this needs no word of commendation. For fifteen years it has been the most satisfactory guide in arranging the preliminary practice on the manikin, which has become an important factor now in every adequate course on obstetrics, before the student begins his clinical training. This new edition is essentially a reprint and presents few changes from the form in which the book first appeared, and none of these changes have any vital bearing on the previous principles laid down. The editor appreciates this and explains that a second edition has been brought out because the first has been exhausted and copies are now obtained with great difficulty and at excessive cost.

The first chapter deals with the anatomy of the pelvic canal and the second with the various positions occupied by the fœtus before and during labor. Following is a description of methods for diagnosis of these positions both by abdominal palpation and vaginal touch. Finally, a thorough and clear consideration is given of the mechanism by which the fœtus passes through the birth canal in natural and artificial delivery.

The text is strikingly perspicuous, and one finds here, as frequently in French works, a gratifying repetition of whatever has gone before that is necessary to a clear conception of the matter at hand. Thus the reader is spared a perpetual search from one chapter to another for facts which properly belong on the page before him.

The student is further aided in gaining a grasp of the subjects by a series of illustrations which it would be difficult to surpass. They are so simple and accurate and in such abundance as to constitute easily one of the distinctive features of the book.

Almost half the volume—one hundred and ninety pages—is taken up with a most admirable account of forceps operations. The impropriety of haphazard application and the great value of adjusting the blades accurately to the sides of the child's head (cephalic method) are clearly demonstrated by word and figure.

The single regret to be expressed is that a translation has not made the work more available for English students.

A Treatise on Obstetrics. By EDWARD P. DAVIS, M. D. Second Edition. (*Philadelphia and New York: Lea Brothers & Co., 1904.*)

A previous edition of this book was reviewed in the BULLETIN. Appreciating the advance recently made in the science and art of obstetrics, the author has brought out a second edition of his text-book, extending the volume of the work and introducing numerous new illustrations.

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CONTENTS.

	PAGE
Cotton Mather's Rules of Health. By Wm. Sydney Thayer, M. D.,	293
Movability of the Heart in Pneumothorax. By W. J. Calvert, M. D.,	300
Endocarditis in Tuberculosis. By Harry T. Marshall, M. D.,	303
A Case of Acquired Cyst of the Conjunctiva containing an Embryonic Toothlike Structure. By Edward Stieren, M. D.,	308
Some Observations on the Occurrence of Micrococcus Zymogenes. By E. G. Birge,	309
Notes on New Books,	311
Books Received,	312

COTTON MATHER'S RULES OF HEALTH.*

By William Sydney Thayer, M. D.,

Professor of Clinical Medicine, The Johns Hopkins University.

Most men take pleasure in the manifestation of a certain playful irreverence toward the worthies of the past. With a perennial naïveté we are fond of patronizing our great grandfathers in a kindly sort of way. We smile at their quaintness and seriousness and ponderousness, while tacitly recognizing our own superior powers of perception and our more delicate sense of humor; and we rejoice in what always seems a deliciously original and somewhat temerarious fancy—that they may have possessed many of our commoner frailties behind that cloak of austerity with which respectful tradition, orthodoxical painters, and fickle fashion have helped to clothe them. And, as a rule, whatever our intentions, we are wont to weigh their lives and actions with scales built of our own contemporary criteria and with little real appreciation of the truth of the observation of the Gallic philosopher that "nothing seems so immoral (to-day) as to-morrow's code of morals," [1] and the converse.

But after all, it is probably well that it should be so. How much of the spice of life we should miss, what a real misfortune it would be if one day, we should find ourselves able to enter wholly into the state of mind of those whose lives as it is, afford us so much cause for beneficent reflection and speculation. The aspiration of Mr. Dinkelspiel who recently gave utterance to the profound thought that "Der vorld vould be much nicer if ve could see udders as ve see ourselfs," would, if realized, result in a very flat world. Moreover, we should not be half as amusing to our descendants. The possession of truth in all things is doubtless precious, but we may, perhaps, be profanely thankful that with our human limitations there is little immediate prospect of being deprived of the greatest of life's privileges, the ever-present opportunity for its pursuit, while posterity is likely, for some time to come, to enjoy the pleasures of complacent contemplation of our inconsequent and entertaining wanderings. It is, perhaps, the part of the wise man in a study of the past, to rejoice in that which is fine, to smile at those contrasts which seem to him quaint and droll and unaccountable, but to hesitate to criticise or condemn.

The reverend Cotton Mather has suffered much from too serious historians who have judged him freely from a nineteenth century point of view. He was born in Boston in 1663. His father, Increase Mather, the leading citizen of New England, was for some years president of Harvard College, while his mother was the daughter of John Cotton, one of the prominent men of Boston. From early youth he was regarded as a remarkable character. He entered Harvard College at the age of eleven and a half, at which time he had already read Cicero, Terence, Ovid and Virgil and could write Latin with ease. He had also read through his

* Read before the Johns Hopkins Hospital Historical Club on March 13, 1905.

[1] "Rien ne semble plus immorale que la morale future." Anatole France, La vie littéraire, 8°, Paris, 1895, III, 74.

Greek testament and had begun Homer, Isocrates, and the Hebrew grammar. In college he mastered Hebrew and composed treatises on logic and physics. He graduated at the age of fifteen and was ushered into independent life with a rather fulsome eulogy uttered by President Oakes as he presented him with his degree; these remarks concluded with the following words: *"Cottonus atque Matherus tam re quam nomine coalescant et reviviscant."*

It is not generally known that in Colonial days the names of the members of the graduating classes at Harvard were recorded neither alphabetically nor according to scholarship but in the order of their social standing.[2] In the Quinquennial Catalogue of Harvard University—that sacred volume to which the late Professor Lane used to refer facetiously, as "the peerage," Cotton Mather's name stands second in the list of the class of 1678, preceded only by that of his cousin, John Cotton. It should, however, be mentioned that the class consisted of but four members.

Suffering from an impediment of speech which it was feared at first might prevent his entering the ministry, he is said to have spent a part of his first two years in the study of medicine, but conquering this infirmity, he began his career as a minister at the age of eighteen. These were days when a young man of ambition started out in life with a firm resolve to excel in many and diverse branches of science, and it may sometimes have happened, if he was endowed with a sufficient measure of self-assurance, that he thought he had mastered them all. Cotton Mather was a man of amazing general information. At the age of twenty-five he is said to have been able to write (*sic*) seven languages, including Iroquois; and of his superior learning and ability there was, apparently, a serene consciousness which the irreverent of to-day might style as knowing it all. His main goal in life appears to have been the presidency of Harvard College, and his failure to attain this was a bitter and nourished disappointment. Conscious of his remarkable attainments and exceptional erudition, Mather appears to have been rather impatient with the rest of the world for a lack of what he deemed due respect and appreciation for his qualities—and he made his fair share of enemies.

Born in an age of implicit and general belief in the powers of Heaven and, especially, of Hell in all its forms, Cotton Mather preserved throughout his life an unshaken faith in the immediate presence of a God who noticed and so forth rewarded every good action, and of a Devil whose malign hand was ever to be detected ready to seize and hold with tightening grasp whosoever was guilty of the slightest lapse from grace. He so trained himself that every common incident of life was, so to speak, a mnemonic for a special prayer or pious ejaculation, and for days together, he subjected himself to fasts and self-mortification such as might compel the admiration of the cloister. To the omnipresent Devil he was a mighty and militant enemy, and no one was so quick as he to detect and frustrate the malicious and insinuating schemes of his subtle adversary. When twenty-five years of age his attention was first directed to the evident manifestations of Satan in the bewitching of the child of a certain Mr. Goodwin of Charlestown by an agent of the infernal regions in the shape of a sharp-tongued old washerwoman who was duly executed for her hellish practices. And his preaching and publications concerning this case doubtless had their effect in spurring on the public to the decisive battle which was waged four years later at Salem against the powers of the invisible world. In this warfare Cotton Mather took an active part. But while tradition has, for nearly a century, pictured him as a relentless inciter of widespread executions, a study of the records appears to show that, active as he was in warfare against his infernal enemies, his voice was usually on the side of cautiousness and humanity, ever raised against the admission of "spectral evidence," and urging a recognition of the possibility that the Devil might manifest himself in the form of an innocent individual. And if, when, in later years, witnesses, jury, and even magistrates were tortured by doubt and self-distrust and remorse, the stern old warrior remained unmoved and defended to his dying day the good fight which he had waged and won against the legions of Hell, it was not so much, as his enemies would have it, an evidence of vanity and cruelty, as that his moderate and humane counsel left him little to regret.

Mather, although he failed to obtain the coveted presidency of Harvard College, was a great power in temporal as well as in spiritual affairs. He had, always, a lively interest in matters medical and was replete with advice and counsel, much of which was good. At the age of fifty-eight, he read, in the Philosophical Transactions of the Royal Society, a paper by Timonius on a "New Method of Introducing Small-pox by Transmission," in which was described the method of inoculation then in vogue in Turkey.[3]

Impressed by the probable benefits which the introduction of this practice might bring to a city in which small-pox was

[2] Quinquennial Catalogue of Harvard University, 1900, p. 83.

[3] The following passage from the Angel of Bethesda would seem to indicate that Mather had already learned of this practice from other sources. "There has been a *Wonderful practice* lately used in Several parts of the World, which indeed is not yet become common in our Nation.

I was first instructed in it by a *Guaramantee* servant of my own, Long before I knew, that any *Europeans* or *Asiaticks* had the least acquaintance with it; and some years before I was enriched with the communications of the Learned Foreigners, whose accounts I found agreeing with that I received of my servant, when he shewed me the scar of the wound made for the Operation; and said, That no person ever died of the *Small-pox* in their country that had the courage to use it.

I have since met with a considerable number of *Africans*, who all agree in *One Story*, That in their country *grandy-many* dy of the Small-pox: But now they Learn This way—: people take juice of *small-pox*, and *cutty-skin*, and putt in a Drop; then by'nd by a little *sicky sicky:* then very few little things like *small-pox;* and no body dy of it, and no body have Small-pox any more. Thus in *Africa*, where the poor creatures dy of the *Small-pox* like Rotten Sheep, a merciful God has taught them an *Infallible preservative.* Tis a *common practice*, and is attended with a *constant success.*"

spreading, Mather urged William Douglas, the leading physician of the town of Boston to put the method into practice. Douglas refused, as did all other physicians excepting a modest young man, Zabdiel Boylston of Brookline, who, on June 27, 1721, inoculated his son aged 13, a negro, and a little colored boy. This was only about six weeks after the introduction of the practice in London at the instigation of Lady Mary Wortley Montagu.

These proceedings caused great public excitement. Almost all the medical profession and many of the clergy violently assailed these two courageous men. Insult and vituperation were poured upon them by pulpit and press, while angry mobs threatened their very lives in the streets. On one occasion, while Mather was harboring, at his own dwelling, a convalescent from the operation, a mob attacked the house and threw a lighted bomb into the room occupied by the patient. Happily the fuse became detached and the bomb failed to explode. Attached to the bomb in such a manner that it might possibly have escaped destruction in the event of an explosion, was the following courteous message: "Cotton Mather I was once of your meeting, but the cursed lye you told of ——— You know who, made me leave you, you Dog. And Damn you, I will enoculate you with this, with a pox to you."

Threats of personal violence continued and Mather sincerely believed that his life was in grave danger. Though his fears may have been exaggerated, yet the following entry made in his journal a few days after the throwing of the "granado" is rather touching evidence of the state of mental exaltation under which he then laboured:[4]

"19/90" (Nov. 1721) "Now, I am so far from my Melancholy Fear on this occasion, that I am filled with unutterable Joy at the prospect of my approaching Martyrdom. I know not what is the Meaning of it; I find my mouth strangely stopp'd, my Heart strangely cold, if I go to ask for a Deliverance from it. But, when I think on my Suffering Death for saving the Lives of Dying people, it even ravishes me with a joy inexpressible & full of Glory. I cannot help Longing for the Hour, when it will be accomplished. I am even afraid almost of doing anything for my preservation. I have a Crown before me; and I now know by Feeling, what I formerly knew only by Reading, of the Divine Consolations with which ye minds of Martyrs have been sometimes irradiated. I had much rather Dy by such Hands, as now threaten my life, than by a Feaver, and much rather Dy for my conforming to the Blessed JESUS in Essays to save the Lives of Men from the Destroyer, than for some Truths, tho' precious ones, to which many Martyrs testified formerly in the Flames of *Smithfield*."

But the old parson and the young physician pursued the even tenor of their way, and gradually gained adherents. In a year Boylston with two other colleagues had inoculated two hundred and eighty-six persons with but six deaths, three of which may have been due to previous contraction of the disease from other sources, while among 5579 uninoculated who took the disease during the same period, 840, or more than one in seven, died. These results ere long, won the day, bringing lasting fame to both at home and honorable recognition in the mother country to the brave physician, Zabdiel Boylston.

Cotton Mather was a most prolific author, publishing during his life 382 works. His most famous publications are: "Magnalia Christi"—an ecclesiastical history of New England, which contains a mass of entertaining and valuable information about the early days of the colony, and his "Wonders of the Invisible World. Being an Account of the Tryals of Several Witches Lately Executed in New England," an amazing exposition of the strategy and machinations of the devil and of the tactics which the servants of the Lord should employ to resist them. Mather was a vigorous writer. He belonged rather to the class described by an author of his own time,[5] who, "with a Supercilious Gravity, have magisterially inveigh'd against the Vices of Mankind" than to the others who "by the nipping Strokes of a Side-wind Satyr, have endeavored to tickle Men out of their Follies." Perhaps there may be some who would class him among what the same author calls the "Sowr Pulpit-Orators."

His invectives against the Vices of Mankind were of no mean force, as the title of his well-known Execution Sermon may suggest. "TREMENDA—The dreadful sound with which the wicked are to be thunderstruck. In a sermon delivered unto a great assembly, in which was present, a miserable African (Joseph Hanno) just going to be executed, for a most inhumane and uncommon murder, at Boston May 25th, 1721."

One can fancy the terror of a superstitious negro on listening to this highly colored discourse, wherein he is apostrophized as "O forlorn Ethiopian," while his crime is referred to as of Ethiopian hue.

Mather's style was most remarkable, consisting, often, of a jungle of strange capitals and italics and Latin quotations interlaced with an exuberant undergrowth of punctuation marks, while in the recesses lurked the furtive anagram and, all too frequently, the Bandar-logian pun. But in the tangled underbrush there is a store of hidden treasure, and in many a passage of his writings there is fine dramatic force and vigor.

Cotton Mather was honored abroad as well as at home. He was made a Doctor of Divinity by the University of Glasgow in 1710 and became a Fellow of the Royal Society in 1713. He died on the 13th of February, 1728, and was accorded a public funeral no less impressive than that of his father in which he had taken a great pride.

[4] The privilege of consulting the manuscript diary of Cotton Mather for the year 1721, which is in the possession of the Massachusetts Historical Society, I owe to the courtesy of Dr. Samuel A. Green, librarian.

[5] The English Theophrastus. 8°. London, W. Turner et al., 1702, Preface.

Among his unpublished manuscripts he left a work entitled:

THE ANGEL OF BETHESDA.

'An ESSAY upon the *Common Maladies of Mankind.*
'Offering, first, The Sentiments of PIETY, where to the
'Invalids are to be awakened in & from their *Bodily* Maladies
'And then, A Rich Collection of *plain* but *potent* and
'Approved REMEDIES for the *Maladies.*
'Accompanied with many very practicable Directions, for
'The PRESERVATION OF HEALTH, to such as enjoy a good
'Measure of so great a Blessing.
'And many other curious, & grateful & useful Entertainments,
'occasionally intermixed.
'The whole being A *Family-physician,* which every Family
'of any capacity may find their Account on being supplied
'Withal.

The manuscript of this remarkable work I have recently had the privilege of inspecting, through the courtesy of the American Antiquarian Society.

In the first chapter the author quotes from a former treatise entitled, "MENS SANA IN CORPORE SANO": "Lett us look upon Sin as the *Cause of Sickness.* There are, it may be, *Two thousand Sicknesses:* And indeed, *any one of them able to crush us!* But what is the *cause* of all? Bear in mind, *that sin* was that which first brought *Sickness* upon a Sinful World, and which yett continues to *sicken* the world, with a world of Diseases: & *Sickness* is in short, *Flagellum Dei pro peccatis Mundi.*"

'Twill be impossible to enter into anything like a full description of this most interesting treatise. A few notes must suffice.

In chapter V, which is entitled "Nishmath Chajim"[6]—the breath of life—there are some striking passages. "It is well known that if *one Third* of our *Diseases,* be those which we call, *Chronical,* more than *one Half* of this Third, will be those, which in *Men* go under the Name of *Splenetic,* and in *Women* go under the Name of *Hysteric;* tho' the *Spleen* and the *Womb* are often enough unjustly accused in these Denominations. It is marvellous to see, in how many *Forms* we undergo *Splenetic* and *Hysteric* maladies; The very *Toothache* it self often belongs unto them: And Marvellous will be the *Success,* Marvellous the *Esteem,* of the Physician that can Discover 'em & Encounter 'em" . . . "These Maladies have many Symptoms, which may serve as *Diagnosticks* for them: Especially these TWO: That the *Urine* is Clear, Limpid, and Copious. And, That the Patient is *Chiefly affected* with his Indispositions, when he has just had his *Mind* under some Disturbance and Affliction."

He advises rest and encouragement, and recommends riding especially, but concludes: "UPON the Whole; OF all the Remedies under Heaven, for the Conquering of *Distempers,* & for the Preservation of *Health* & Prolongation of Life, There will now be found none, like serious PIETY." and "LET this be Remembered; Moderate *Abstinence,* & Convenient *Exercise;* and some Guard against Injurious *Changes of the Weather,* with an HOLY & EASY MIND, will go as far, in Carrying us with *Undecay'd Garments* thro' the Wilderness, to the Promis'd and Pleasant Land, which we are Bound unto, as all the *Prescriptions* with which all the Physicians under Heaven, have ever yet obliged us."

There is an excellent chapter on "The *Gymnastick* or an Exercitation upon EXERCISE," which contains much wisdom. Of riding, which he commends especially, he says: "*If a man knew, and would keep to himself,* any Remedy equal to that of a Course of *Riding, Opes ille exinde amplissimas facile accumulare posset,* he might soon come to keep *a coach* and know ye English of *Doct Galenus opes.*

"I hope the *Rider* in the meantime, won't be unmindful of Darby Dawn's caution,

> *But lett the Rider take a care;*
> *Lest from a stumbling Horse or Mare*
> *He don't take Earth instead of Air.*

Chapter VII is in some respects, the most interesting of the work; it is entitled: "Conjecturalia or, Some Touches upon, A *New Theory* of many *Diseases.*" Quoting various authorities, he expresses the belief that a large number of diseases, among which are Small-pox, Plague, Consumption, Lues, bad colds and the itch, are due to infection with minute parasites which may be transmitted by the air or, under some circumstances by contact with the patient. He refers to these parasites which, he says, may be too small to be visible by the best microscope as "insects" or sometimes as "worms"; the chapter ends with the following paragraph: "But, O ye Sons of erudition, and ye *wise men of Enquiry;* Lett this *Enquiry* come into a due Consideration with you; How far a potent *worm-killer,* that may be safely administered, would go further than any Remedy, yett found out, for the cure of many Diseases."

In chapter XII he refers to the Gout as "*Dominus Morborum;* But especially, *Morbus Dominorum,*" and offers the following consoling advice to the gouty: "Now, lett ye *gouty* People that are *chastened with Pain on their Bed, and the multitude of their Bones with strong pain,* fall into serious and awful *Meditations,* on ye pain, which will be ye portion of them, on whom an All-powerful God will make known the *power of His Anger!*"

Chapter XIII is on "The *Gout's* Younger Brother or, The *Rheumatism,* and *Sciatica.*"

In chapter XX, on Small-pox, the interesting story of the introduction of inoculation is told.

In the section on diseases of the eye he waxes eloquent: "SPECTACLES! Mankind is prodigiously inexcusable, in

[6] This chapter has been published in book form. "Nishmath Chajim. The Probable SEAT of all Diseases, and a General CURE for them, further Discovered. More particularly, for *Splenetic & Hysteric* Maladies, which make so great a part of our Distempers." New London, 1722.

that the Name of ye First Inventor is entirely lost. That statues of *Corinthian Brass* have not Immortalized it."

Chapter XLII is entitled: "*The Main Wheel Scoured & oiled*" or, Help for the *Stomach* depraved."

The peritonitis which, in most cases doubtless represented appendicitis, is described unwittingly, in a manner which would have delighted the author had he realized what he was doing, in an appendix to the chapter on Cholic, in the following words: "A grievous and fearful Disease, an Appendix to the *Cholic,* is now broke in upon a miserable world; called, The Dry-Belly-Ache." . . .

"Under the Torments of this horrible Disease, we may recommend unto the patient such sentiments of PIETY as we found the *Cholic* leading to." . . .

"In so Difficult a case, and where so wise a Conduct is required I dare not offer any prescription, but, *A Wise Physician.* Consult such an one and follow his Directions, relying wholly on ye Blessing of God."

The small volume which I have this evening, is entitled "Manuductio ad Ministerium or DIRECTIONS for a Candidate of the MINSTRY. Wherein, FIRST Right FOUNDATION is laid for his Future Improvement; And, THEN, RULES are Offered for such a Management of his *Academical* and *Preparatory* STUDIES; And thereupon, For such a CONDUCT after his APPEARANCE in the World; as may Render him a SKILFUL and USEFUL minister of the Gospel." This work was published in Boston, "Printed for *Thomas Hancock,* and sold at his shop in Ann-Street near the Draw-Bridge" in 1726. It is dedicated, in Latin, to the studious youth of the academies especially in Glasgow and in New England as well as to any young non-conformists in England compelled to work in private.

After a learned Latin introduction, he holds forth to his readers in twenty chapters upon various subjects, such as:

§1. DEATH Realized.

§2. The True End of Life Answered.

§3. Conversion to Piety accomplished &c.

The last chapters are RULES OF HEALTH and RULES OF PRUDENCE. There is so much that is wise and quaint and entertaining in these pages that I shall read the whole chapter, entitled: RULES OF HEALTH and a few extracts from his even more admirable RULES OF PRUDENCE:

"§19. I have yet more to do; I may not leave you, till I leave a few RULES OF HEALTH with you; which I shall do with the utmost Brevity.

"Having first encouraged you to cultivate an intimate Acquaintance with some Wise and Good *Physician,* who may have the continual *Inspection of your Health,* in your Friendly Conversation with him, I will defend you with the ensuing Admonitions.

"I. The most Acute Physicians, find themselves compelled, with our *Cheyne,* unto this General Direction. The *Grand Secret* and *Sole Method* for *Long Life,* and so for the *Health* which will befriend and sweeten it, is, To keep the *Blood* and *Juices* in a State of due *Fluidity.* And nothing will do this, but keeping much to a *Spare, Lean, Fluid* sort of a *Diet.* All who *live long,* and without much *Pain,* and after such a Life at length *Die easily,* are such as Live *Abstemiously.*

"II. *Borellus* has a Remark on many Students falling into a *Consumption,* That it often proceeds, *A Fumo candelarum hausto in Musaeis undiq; Clausis.*

"You will undergo the less of this Hazard, if you mind the Report of *Manlius; Ego multos Periculosos Morbos et Miserias hujus Corpusculi mei Vito, hac unica Ratione, quod semper utor Diligentia, cito eundi cubitum.*

"III. The *Medicina Gymnastica* has done Miraculous Things. *Bodily Exercise profits;* But no *Exercise* comparable to that of *moderate Riding;* whereof, the Reason why we find no more in the Prescriptions of the Ancients, (tho' *Galen* has a Chapter about it) for the Recovery of the Feeble, is because they were so simple as to *Ride without Stirrups.* The *Saddle* is the *Seat of Health.* As for the *Games,* which Exercise the *Spirit* and not the *Body,* particularly, the Noble and Ancient Game of *Chess;* These are by no Means proper for a *Student.*

"IV. 'Tis an Observation of that Great Man, the Lord *Verulam, Nihil magis conducit ad Sanitatem et Longaevitatem, quam Crebrae et Domesticae Purgationes.* A *Family-Purge* now and then taken, may be of Service to you. *Pillulae Ruffi,* especially when Chalybeated with adding about a third part of *Sal Martis:* Or else; A Bottle of *Anniseed Water,* with a *Dram* or two of *Rhubarb* steeped in it; These you may conveniently have always at hand for this Purpose.

"V. *Vander Heidan,* has not related an hundredth part of the Vertues, in *Cold Water.* I tender you the Advice which the Aged Servant of GOD gave to his Valued Son, *Drink not only Water; but use a little Wine for thy Stomach's sake.* And yet I would say, upon Drinking a Glass of Generous *Wine,* often take a Glass of *Water.* And if the *Beer* they bring you, be too *Strong,* dilute it with putting a sufficient Quantity of *Water* into it. But never take *Water,* or any thing else, *Cold,* when you are *Hot* with Labour. There is *Death in the Pot.*

"When you have run the hazard of disturbing your *Stomach,* with Ingurgitations from a Full Table, a Draught of *Cold Water,* will do *Good like a Medicine.*

"Going to Bed, and Sweating from a large Draught of *Cold Water,* not only stops and cures a *Cold,* but also often extinguishes a *Fever* at the Beginning.

"Daily to wash your Head and Mouth with *Cold Water,* is a Practice that cannot be too much commended; If it were o ly for saving you from the *Toothache.*

"For a Frequency in the Use of the *Liquors,* which they call *Spirits,* be as afraid of it, as you would be of a Familiarity with *Evil Spirits.*

"VI. When you go to Infectious Places, one of the best Things you can do, is to hold and chew a bit of *Myrrh* in your Mouth.

"VII. To feed much on *Salt-Meats,* won't be for your

Safety. Indeed, if less *Flesh* were eaten, and more of the *Vegetable* and *Farinaceous* Food were used, it were better. The *Milk-Diet* is for the most part some of the wholesomest in the World! And not the less wholesome, for the *Cocoa-Nutt* giving a little Tincture to it.

"VIII. *Shall I smoke Tobacco? Answer;* Be sure *Not,* if I can help it. Or let *Alsted* answer for me. *Maximus Tabaci Abusus est, quotidiano ejus usu, semetipsos, et bonas Horas perdere, et ex cerebro, mentis nobilissima sede, caminum et cloacam efficere.* In the Dutchy of *Berguen,* People may not *Smoke,* without purchasing a *License* for it. If you were to purchase of me a *License* for it, I know not how high Terms I should hold you to. If you want an *Hydragogue,* there is one preferrible in chewing some such Thing as a bit of *Mastich;* which would also whiten your *Teeth, and* sweeten your *Breath,* which *Tobacco* poisons. If once you get into the way of *Smoking,* there will be extreme hazard, of your becoming a *Slave* to the *Pipe;* and ever *Insatiably craving* for it. People may think what they will; But such a *Slavery,* is much below the Dignity of a *Rational Creature;* and much more of a *Gracious Christian.* I am sure, what the Great *Voetius* writes upon it, is very true; *Minime convenit viris honestis et gravibus; nominatim Ministris et Ministerii Candidatis.* There can be no *Apology* for your taking up the *slovenly Practice,* and the Pains that must be taken to conquer the *Poison,* if you are not well advised and assured, *That your Health requires it.* But I shall only recite what you will find in Two very considerable Writers, that you may form the better Judgment upon it. The One of these Writers is *Magnenus,* who tho' he be a mighty Friend to the Use of *Tobacco,* yet acknowledges, 'That it is not easy to relate, 'what are the *Damages,* which the Inordinate and Immoder-'ate Use of this *Fume* does bring with it; for besides the in-'satiable and greedy Lust of taking it, by its *daily Use,* the '*Memory* is impaired, the *Stomach* violated, the *Brain* exic-'cated, and the *Life* shortened; and the *Offspring* damnified. Yea, he lays this down as an undoubted Assertion; *That the frequent and familiar Use of it, can be good for no Man.* The Other is our *Gale,* who from his own Experience taxes the Smoke of *Tobacco* with very *Noxious Qualities:* He says, 'He found it *made* more Humours than it brought away; 'and tho' it *opened* his Body for the present, it proved in that 'very thing a Prejudice afterwards; and Nature was but the 'more Sluggish and Feeble anon, for the *Force* in this way 'put upon it. He says, At last *I came under a fixed Resolution to deliver my self from this Vassalage; And this I account not the least Deliverance of my Life.* And yet, after all, I am not so *Inflexibly sett,* as utterly to deny you the Use of *Tobacco,* if you are sure of any *Benefit* from it. Only I insist upon it, That you be, (If I may use a *Phrase,* that if it may seem to trespass upon *Good sense,* it shall yet have as much as the *Thing* I write against) *Excessively Moderate* in it. And if you are growing so Wise as to Retrench and Reform any *Intemperance* in it, which you may have been unawares drawn into, do it not *at Once,* but *by Degrees,* lest by too quick a stop to an *usual Discharge,* your Health may be endangered. But, upon the whole; If you have hitherto escaped this *Epidemical Contagion,* and are not yet a settled Inhabitant of the *Terra del Fuogo,* I cannot advise you in better Terms than those; *It is Good for you to abide even as you are;* And, *If you may be kept free, chuse it rather.* Yea, *My Son, If* Smokers *entice thee, consent thou not.* It is good Advice; and if you take it, you will one Day Thank him that gavé it.

"But if I am against your taking *Tobacco* in *Smoke,* you may be sure, I shall not approve your taking it in *Snuff.* How *shameful* a thing it is, for *People of Reason* to confess, that they can't live easily half an Hour together, without a *Delight* so Sensual, so Trivial, so very Contemptible, as that of *Tickling their Olfactory Nerves* a Little? And even *bury* themselves alive, in *pungent Grains of titillating Dust?* A Learned Physician of the *French* Nation, will tell you, how many Diseases of the *Genus Nervosum,* do issue out of that *Pandora's Box,* from whence the Pinch of *Snuff* is taken. A *Quincy* will tell you, how wretchedly it *spoils the Appetite.* And a *Cheyne* will tell you, how much the *Eyes* as well as the *Stomach* fare the worse for it. You may dream, that the Passage thro' the *Os Cribriforme* will not permit the *Gross Powder* of your Snuff to enter into your *Brain;* yet some very thin and fine Parts of it will find their way thither. And what Mischiefs must needs follow a *Brain* so poisoned? Nay, One would think, that the great *Snuff-takers* had their Brain already touch'd; or they could not be so obstinately and incurably attach'd unto an *Evil Habit,* which their Folly has brought upon them. A very just Motto for the *Snuff-box* might be, A LEADER TO THE COFFIN. If it be offer'd you, *Away with it!* I say again, *Away with it!*

"IX. A Knight of my Acquaintance visiting the famous Dr. *Lower,* in his last Sickness, ask'd him for the best Advice he could give him, *How to preserve his Health, and prolong his Life;* the Doctor only answered him, *Don't eat too much!* After some other Discourse, the Knight not imagining that the Doctor had thoroughly answered his Enquiry, repeated it. The Doctor thereupon only repeated his Answer, *Why, Didn't I tell you; Don't eat too much!*—And, *further said not.* Sr. *Theodore Mayern* on his Death-bed gave this Advice to a Noble Friend, that ask'd his Counsil for the preservation of his health. *Be moderate in your Diet; Use much Exercise, and little Physic.* I would have added, *Guard against injurious Changes of the Weather; and especially be exposed unto the Night-Air as little as may be.*

"X. *Baglivi* is not the only Gentleman, who has observed, how much *Tranquillity* and *Serenity* of the *Mind,* contributes unto the *Health.* Hofman in his Treatise, *Des Moyens de vivre Longtemps,* has observed, That in the way of keeping the *Mind Quiet,* the *Fear of the Lord tends unto Life.* An *Holy* and an *Easy* Mind, is the most *Healthful* Thing under Heaven: The most potent *Prophylactic* in all the World. I need say no more.

"Only This. Forever *Obsta Principijs.*—If any Sickness

come upon you, be sure to be *Sick soon enough.* Maladies taken at the Beginning may be easily and presently conquered; when—*Delays are dangerous.* And if you are upon a Recovery from any Malady, *Ben't Well too soon!*

"20. I have now no more to do; but only single out a Few RULES OF PRUDENCE, the Observation whereof may be your Preservation from very many Wrong Steps, in the Way you have now before you. It cost the *Prussians,* the Trouble of a *War,* before they could oblige their Neighbours, to call them no longer *Brutos,* which they did before the Tenth Century, but, *Prussos,* which signifies, it seems, *A Prudent People.* I wish it may cost you no more Trouble, than only a little *Reading* of, and *Thinking* on, certain *Maxims of Prudence* to render you one of that People. I shall not say, how much it has *cost* me, and what a *Dear-bought Experience* it is, that has enabled me to recommend them. . . .

"I. The *Italian* Maxims are no *Imprudent* ones. One must not *Spend all he hath;* nor *Do all he can;* nor *Tell all he knows;* nor *Believe all he hears.*

"And there is a Sentence of a *Greek* Poet, worthy to be remembred with you; which in plain *English* will tell you, *No wise Man will be taken a second Time, in an Error he hath suffered for.*

"II. It is a Lesson worth more than an Ingott of Gold, which one who *saw many Things,* has left, for what is to be uttered in Company; *Bis prius ad Limam quam semel ad Linguam. Think* before you *Speak; Think* before *whom* you Speak; Think *why* as well as *what* you Speak. And Remember, *In multiloquio Stultiloquium;* And *Least said soonest mended.*

"It is a very prudent Remark; If one observes these Three small Imperatives, *Audi, Cerne, Tace,* he will need no other Passport for Travelling over the World. You will have a good Note of Wisdom, with two *Satellits* to it, in my reciting to you the Observations of a very Discrete Man, who said; *He had often got hurt by eating too much; rarely, by eating too little; Often got hurt by wearing too few Cloaths; rarely, by wearing too many; Often got hurt by Speaking; rarely, by holding his Tongue.*

"VII. Let it be as a *Law of the Medes and Persians* with you, *That you will never sacrifice any Hours of a short Life,* in *Contentions:* Especially in *Personal* Contentions, and Quarrels and Squabbles, and *Vitilitigations. Abundance* of Sin will be unavoidably committed in them; And, *The Game will not pay for the Candle.*

"IX. Don't Use your *Pen,* and Lose your *Time,* in *Eristic Writings,* any more than unquestionable *Duty* and *Prudence* makes to be absolutely Necessary. Writing upon a Point, and in the Way and Strain of *Controversy,* will not only have a Tendency to discompose the *Peace* of your Mind, but miserably Divert the *Studies* of a short Pilgrimage, from such things as would be much more Profitable for your self and others. Anon, the *Grand Point* of the *Controversy* will be, only *Who has most Wit or Grace of the Two,* you, or your Antagonist. A *mighty Business!* If *Jerom* were pleased in an Hectoring way to forewarn his Opponents, that he was, *Cornuta Bestia;* I hope *you* won't be so.

"X. If Calumnious *Quills* have publickly scratched you,—*An Respondendum semper Calumniis?*—No. Look as far back as Two Thousand Years ago, and you will find even a *Plato* giving a Pattern to a Christian, in his declining to take any Notice of the Invectives which a *Xenophon* had used upon him.—It may be, the *Scribblers,* are sorry *Scoundrels,* and such vile *Children of Sheth,* as it is beneath you to let them know that you have so much as read their Follies.—Or be they what they will, *for the most part,* the best way will be to, *Shine on,* Regardless of what the *Batts* and *Owls* may mutter against you. Or, if that Metaphor be too *Sublime,* let me say, At least *As the Moon among the lesser Fires,* keep a steddy Pace, *Walking in your Brightness,* notwithstanding the unregardable Allatrations of your Adversaries. If they persecute you with *Libels,* 'tis a notable Hint, that *Le Clerc* has given you. Instead of answering them, write such learned and useful *Books,* as will be of *perpetual Service* to Mankind. These will procure such a casting and lasting *Testimony* for you, that there will need no more to make a Man ill tho't of, than this; That he was a *Thersites* to *you,* and one that wrote against you. These *Books* will be durable Monuments of your Valuable and Honourable Character, when the Libels of these poor *Animalculicuncles* will perish among the *Wast-Paper,* which the *Haberdashers of small Wares* have occasion for.

"And if any *Preacher* should be so impertinent as to have any Girds at you in the Pulpit, remember the Advice of the sweet-spirited *Melancthon* to *Vitus Theodorus,* when the hot-spirited *Osiander* had preached against him; *I charge you, Don't Answer the Man; Hold your Peace; Go on in your Ministry as if you had heard nothing!*—The Gentleman soon found his Account in hearkening to his *Candid* Adviser.

"That what I am driving may stick, you shall have it in the Form of two old Rusty Nails; The One, *Magnum Contumeliae Remedium Negligentia;* The other, *Sile, et funestam dedisti Plagam.*

"As wicked a Fellow as ever polluted a Pen, yet has this Passage worth transcribing from him, while his Name is not worth mentioning. 'The Malice of *Ill Tongues* cast upon 'a *Good Man,* is only like a Mouthful of *Smoke,* blown upon 'a *Diamond,* which tho' it clouds its Beauty for the present, 'yet it is easily rubb'd off, and the Gem restored with little 'Trouble to its Genuine Lustre. But an *Honester Pagan* than he, has told you, *Perditi Hominis profligatique Maledictis, nullius Gloria dignitasq; Violatur.* Old *Cicero* tells you so. . . .

"XII. While you are yet in your *Younger Years,* be always furnished with a Stock of Weighty and Useful *Questions.* By wisely and humbly offering These, and with the Modesty of One desiring to be Instructed, you may commonly *lead* the Conversation, even with your Superiours, & almost necessitate a *Profitable Conversation.* You may be, as *R. Jeremy*

was called, *The Master of the Questions.* A *Discretion* in this point, is a distinguishing Thing. But whenever you are *Arguing,* ordinarily propose every Thing rather *Socratically* than *Dogmatically.* Be not *Positive;* much less *Clamorous;* least of all *Furious.* But keep up an Air of *Modesty,* and carry on your Discourse, in the form of proper *Questions;* and as one willing to be *instructed* by him whom you are disputing with. 'Tis an *Excellent Wisdom,* this; To *Argue Handsomely.* . . .

"XVII. If you have laid up an Inexhaustible Store of *Stories,* accommodated unto all the Purposes of the *Profitable* and the *Agreeable,* and have the Skill of *telling* them *Handsomely,* and with a *Deliberate, Expressive, Unstumbling Brevity,* and produce them on many occasions, you may not only *Ingratiate* yourself wherever you make your Appearance, but also obtain almost any *Request* that you shall make one of *them* a *witty Introduction* to. The *Precious Stones* that every one sets a Value on, are called *Pleasant Stones.* But let not your *Pleasancy,* degenerate into any unbecoming *Levity.* Forever so *Regulate* it, and so *Moderate* it, that it may *Gracefully Terminate* in the most *Serious Discourse,* and if it may be, in the Inculcation and Insinuation of some *serious Maxim,* which may be *Good for the Use of Edifying.* . . .

"XIX. It may not be amiss for you to have *Two Heaps.* An *Heap* of UNINTELLIGIBLES; and an *Heap* of INCURABLES. Ever now and then you will meet with something or other, that may pretty much distress your Thoughts; But the *shortest Way* with the Vexations will be, *To throw them into the Heap they belong to,* and be no more distress'd about them.

"You will meet with some *Unaccountable* and *Incomprehensible Things;* particularly, in the *Conduct* of many People. Throw them into your *Heap of Unintelligibles;* leave them there. Trouble your Mind no further; *Hope the Best,* or *Think no more* about them.

"You will meet with some *Unperswadeable* People; No Counsel, no Reason will do any Thing upon the *Obstinates:* Especially, as to the making of due *Submissions* upon Offences. Throw them into the *Heap of Incureables.* Leave them there. And so do you go on to *do as well as you can,* what you have to do. Let not the *Crooked Things that can't be made streight,* encumber you.

"XX. 'Tis a Trespass on the *Rules of Prudence,* never to know, *when to have done.* Wherefore, *I have done!*"

MOVABILITY OF THE HEART PNEUMOTHORAX.

By W. J. Calvert, M. D.,

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C. C. L., white, American, male, age 19, student, came to Parker Memorial Hospital, medical service, February 6, 1905, complaining of pain in left side.

Family history strongly tuberculous.

Past history.—He has had the ordinary diseases of childhood, otherwise has enjoyed good health; has been sick in bed three weeks since Christmas but lately has been better. This a. m., about 10 o'clock, he had a sudden giving-way, sharp pain in left side, and sudden shortness of breath, increased on slightest exertion.

Physical examination.—Inspection. Left side is much larger than right; intercostal spaces obliterated; movement diminished as compared with the right side. Upon the left side movement was almost entirely confined to the upper three ribs, where it was increased. Lower portion of left thorax was almost motionless. Apex beat not visible. Palpation revealed a diminished vocal fremitus in upper front and axilla, and absence of vocal fremitus in lower front and side. In back vocal fremitus was diminished. No apex beat felt on the left side. Percussion gave a tympanitic note over entire left side from left border of sternum to posterior axillary line. In back the note was more resonant. Dull about the seventh rib. The boundary of left pleural sac could easily be traced by the tympany, which in the lower portion of thorax was of a different pitch from that of the stomach. Lower border of left pleural cavity was in the mammary line at the lower border of eighth rib, anterior axillary line at upper border of ninth rib, mid-axillary line at upper border of tenth, and in scapular line at upper border of eleventh rib. No heart dulness to left of sternum. Diaphragm evidently pushed downward. Auscultation gave diminished respiratory sounds with few moist râles on inspiration. Once or twice an amphoric quality was noted in the respiratory sounds.

Right side. Movement increased, equally distributed over entire side. Heart beat noted in fourth and fifth interspaces at right border of sternum. Heart beat palpable. Vocal fremitus increased. Percussion note was slightly higher than normal, respiratory sounds loud, slightly roughened, and an occasional râle. Liver dulness normal. Splenic dulness was obliterated, organ not palpable.

Heart. Apex beat to left not visible or palpable; to right, heart beat was visible and palpable in fourth and fifth interspaces at right border of sternum. Dulness to left of sternum completely obliterated even on deep percussion. To right, heart dulness extends from third to sixth rib. At lower border of third rib heart dulness is three and one-half; at upper

border of fourth, four and three-tenths; at lower border of fifth, five and one-half centimeters to right of mid-sternal line. The angle between the right border of the heart dulness and liver dulness is acute in place of a right angle. On auscultation the heart sounds to the left of the sternum could be faintly heard and appeared as if far away, while on the right side they were distinct and sounded as if they were just under the skin. In character, they were rapid, varying from 108 to 148 per minute, weak, clear, and free from murmurs. The second pulmonic was slightly accentuated. When the patient leaned forward the heart fell forward against the left anterior thoracic wall with a bound which could easily be felt. The apex beat could then be easily felt and seen, and the sounds appeared just under the skin, as described for the right side of the sternum. Apex beat was midway between the para-sternal and mammary line. No murmurs were heard. When patient assumed a dorsal position the heart fell backwards away from the left thoracic wall when the heart sounds to the left of the sternum became distant as before.

Once during the course of the disease fluid was thought to be present in the thorax, but positive signs were not obtained. A movable dull tympany was noted in the lower portion of the cavity but no further signs were observed. Judging from the subsequent history, fluid was never present. On puncture air alone was withdrawn.

The patient remained in hospital twenty-three days, during which time very little change in signs was noted from day to day. Temperature never went above 101° F., and dropped to normal during the first week in hospital. The percussion note, etc., remained practically constant until towards the close of his stay, when all the signs began to disappear. The note became resonant at the apex and gradually extended downward, the heart dulness began to be noticed to left of sternum and gradually extended almost to mammary line, and the pulse became normal. When examined about two weeks after leaving hospital a large rough friction sound could be heard in the lower portion of the left side. It suggested a lung hanging loose in the pleural cavity and bounding from place to place against the thoracic wall. At this time no signs of fluid were present. Pulse was again rapid. Heart dulness was slightly to right of sternum. There was no fever; no dyspnœa, except on undue exertion, and at no time were tubercle bacilli found in sputum.

Examination, March 23. The lung completely fills the pleural cavity. There are no pleural rubs and but few moist râles on inspiration. The heart dulness extends to one-half centimeter inside the left nipple line, no dulness is elicited to right of sternum. The pneumothorax has entirely disappeared.

Diagnosis.—Pneumothorax without effusion—recovery.

The forward and backward movement of the heart observed in this case is commonly seen in hydro- and pneumo-pericardium; but in the literature at hand has not been recorded in pneumothorax of the left side. On careful examination of this case hydro- and pneumo-pericardium were excluded. In these the sac is distended with either water or air, which permit the heart to sink by gravity toward the lower side. Consequently an explanation of this heart movement is necessary. In pneumothorax of the left side, the factors essential to this movement of the heart are a change in size and position of the pericardium, change in position of the left lung, pleura filled with air, and the intra-pleural pressure.

The pericardium is firmly attached above and behind to the right of the vertebral column, to the large blood-vessels, as is shown in Figs. 1 and 2, and below to the diaphragm, as is shown in Fig. 1. The movement of the pericardium about its attachments is limited. Consequently any change in position of the pericardial walls must be associated with a change in position of the large blood-vessels, the diaphragm, by stretching of the wall itself, or by a combination of two or

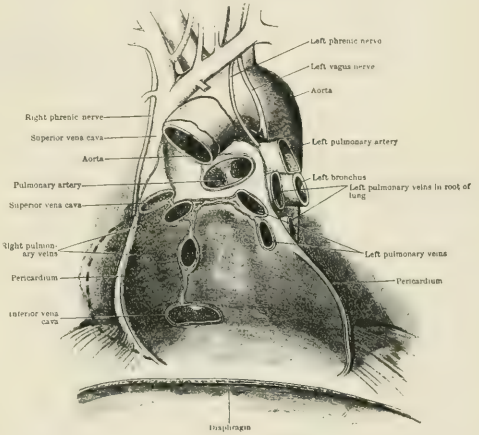


Fig. 1 is reproduced from Cunningham's Anatomy, Fig. 551. It shows the pericardial attachments to the diaphragm and large vessels, and the attachment of the heart to the large veins behind and to the right of the median line. The dotted line to the right is intended to show the displacement of the right wall of the pericardium by the pressure from the left pleural cavity.

more of these factors. From above and behind the heart swings free in the pericardial sac toward the left side, as shown in Fig. 2, swinging about its attachments, as a hinge, in whatever way gravity may carry it.

The heart is held in position by the pericardial sac, the large vessels attached to its base, and by the lung supporting the pericardial sac. If the lung is collapsed the pericardial sac will not retain the heart in its normal position.

In pneumothorax of the left side, in the absence of pleural adhesions and extensive consolidation, the lung collapses and falls toward the posterior portion of the pleural cavity, usually lying on the posterior thoracic wall next the vertebral column. In this case the lung was directly against the posterior thoracic wall, shown by the defective resonant note in the back.

Consequently the lung offered no support to the left wall of the pericardium. The movement of the heart toward the right in left pneumothorax is one of the earliest signs. The pressure on the left wall of the pericardium pushes this wall by the intra-pleural pressure. On account of the displacement of the heart to the right, the left wall of the pericardium is made more lax than normal. The pericardial sac is enlarged in proportion to the displacement of its right wall.

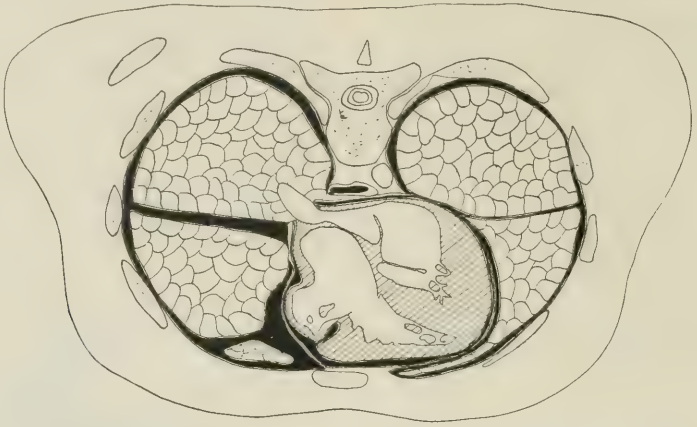


FIG. 2 represents a cross section of the body passing through the heart and lungs, and shows the attachment of the heart posteriorly and to the right of the median line. This picture was copied from an unpublished drawing made by Dr. C. M. Jackson, professor of anatomy, University of Missouri.

against the heart which transmits the pleural pressure to the right wall of the pericardium. This wall must support the pressure in the left pleural cavity. On account of this pressure the right pericardial wall is displaced toward the right

But, on account of the intra-pleural pressure the pericardium is collapsed and in contact with the heart. In hydro- and pneumo-pericardium the pericardium is enlarged and distended by the intra-pericardial pressure. The pleural cavity

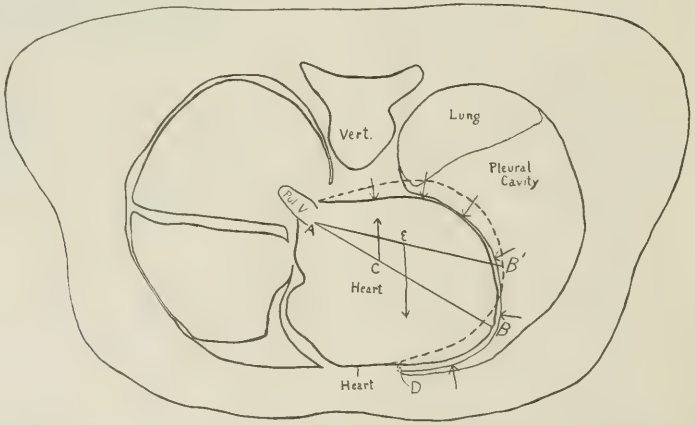


FIG. 3 represents a cross section of the body at the same level as Fig. 2. The collapsed lung is shown in the posterior portion of the pleural cavity. The dotted line represents the heart when patient is in the dorsal position. The heart is not shown to right of sternum.

to a point where the elasticity of the pericardial wall equals the pressure from the left pleural cavity, Fig. 1, dotted lines. The heart follows the right pericardial wall toward the right, and the left pericardial wall is kept in contact with the heart

passes both in front and behind the pericardium. The intra-pleural pressure is directed at right angles against the pericardium, Fig. 3, arrows. Consequently the pressure from behind will equalize the pressure from in front, leaving only

the pressure directed from left to right to interfere with the backward and forward movement of the heart. When the body is in the dorsal position gravity acts on that portion of the heart to the left of its attachments to the large blood-vessels at an acute angle to the line *AB*, seen at *C*, Fig. 3. Unsupported by the lung, and in an enlarged pericardium, the heart falls backward away from the anterior thoracic wall to *B'*. The intra-pleural pressure keeps the pericardium in contact with the heart and separated from the thoracic wall, as shown at *D*, Fig. 3, dotted lines. When the body is in the ventral position, gravity acts on the heart at nearly a right angle to the line *AB'*, shown at *E*, Fig. 3. Consequently the heart falls forward to *B* and is against the anterior thoracic wall. The pericardium is now separated from the thoracic wall by the pleura. Consequently the heart beat may be seen and felt, dulness elicited, and sounds easily heard. When the heart is at *B'*, the apex beat may not be seen or felt. The dulness is absent. The tympanitic note is the same as in other areas of thorax, probably on account of tension of thoracic walls. The heart sounds are distant and indistinctly heard.

In hydrothorax with complete collapse of the left lung this movement of the heart should be present; however, with partial collapse sufficient support would be given to maintain the normal position. In either hydro- or pneumothorax with pleural adhesions, this movement of the heart cannot take place. Consequently, in the absence of hydro- or pneumopericardium, this backward and forward movement of the heart becomes an important differential sign between pneumothorax and a moderate degree of hydrothorax. As a pleural cavity greatly distended with fluid would rarely be mistaken for pneumothorax, this movement of the heart may be considered one of the positive differential signs in pneumothorax.

ENDOCARDITIS IN TUBERCULOSIS.[1]

By Harry T. Marshall, M. D.,

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The cases in which endocarditis and tuberculosis occur together may be divided into three main classes: I, endocarditis preceding tuberculosis; II, endocarditis arising in tuberculous patients but not produced by the tubercle bacillus; and III, endocarditis resulting directly or indirectly from the action of tubercle bacilli. This is practically the classification proposed by Anders in 1902.

I.

Endocarditis Preceding Tuberculosis.

For many years the view was held that tuberculosis does not attack the endocardium, and that tuberculosis and endocarditis are mutually antagonistic, and do not occur concomitantly. This latter view, advanced in 1855 by Rokitansky, obtained a large following. It was supposed that a valve lesion, by causing a congestion of the lungs, acts in some way to prevent the development of tuberculosis. Rokitansky stated the hypothesis that "Persons laboring under enlargement of the heart (dilatation, hypertrophy, and their complications), whether primary or superinduced by mechanical obstruction at its orifices, do not contract tuberculosis." He also held that any other condition producing cyanosis had the same influence, and that cyanosis was a complete protection against tuberculosis.

This hypothesis, which was supported by finding how rare tuberculosis is in mitral disease, as compared with its relative frequency in aortic disease, obtained the not unqualified approval of the clinicians.

Rokitansky's doctrine was successfully attacked by Frommhold in 1875, who, in studying 277 cases of heart disease, found 22 (8 per cent), with pulmonary tuberculosis, the left side of the heart being affected in all but one instance. Since this observation there have been many others in which the heart has been found affected in tuberculosis in varying percentages, thus: Birch-Hirschfeld found chronic pulmonary tuberculosis in 20.8 per cent of 4359 routine autopsies, while in 107 cases with lesions of the heart valve, tuberculosis occurred only 5 times (4.6 per cent). In 2 cases with pulmonary stenosis there was pulmonary tuberculosis. Krygen had 10 cases of endocarditis in 1100 autopsies on tuberculous patients, 4 showing aortic insufficiency, 3 mitral insufficiency, and 2 pulmonary stenosis. In Osler's series of 216 autopsies on patients dead of phthisis, 12 presented a fresh endocarditis. Of these the mitral valve was affected 8 times, the aortic valve 3 times, the aortic and mitral once. One case was an ulcerative endocarditis, the other eleven, verrucose. Kidd reports finding heart lesions in 27 cases out of 500 autopsies on phthisical patients, one of these was a fibrous myocarditis, one a chronic endocarditis, the others apparently were fresh endocarditis, in 10 cases being on valves showing chronic changes. In nearly all of the cases showing chronic lesions there was a history of rheumatism. In over one-half of his series he was uncertain whether the tuberculosis or endocarditis was the primary lesion, nor could he find any definite relationship between the two processes. Potain (Semaine Méd., 1892) found phthisis 9 times in 54 cases of mitral disease. Anders reports 6 cases, 4 with mitral insufficiency, 2 with mitral stenosis. He had no cases of aortic valve disease with phthisis, but he obtained one each of aortic stenosis, and aortic regurgitation out of 40 cases which he collected. This is not the usual experience, as Traube and others found the lung trouble oftener associated with aortic disease than with mitral disease.

[1] Read before The Lænnec, March 22, 1905.

Anders concludes from his review that "the association of phthisis with primary valvular heart disease is probably more common than the usual clinical findings have thus far indicated." It seems, however, fairly clear that tuberculosis develops less often in patients with left-sided heart disease than in others. Graham attributed this relative immunity to: 1st, increased amount of blood in the lungs; 2d, greater expansion of the apices; 3d, increase of the involuntary muscle fibers of the bronchi.

Abrams noted that while patients with endocarditis and tuberculosis did well as long as compensation was maintained, when compensation failed the tuberculosis became fulminating, and he denied the value of congestion, insisting that the protection came from the cardiac hypertrophy.

Anders reviews the literature upon the changes in the symptoms of phthisis resulting from left-sided heart disease. Of these an increased tendency to hemoptysis is the most striking, and this bleeding returns frequently, and at times is very profuse. Dyspnœa is increased and is of the cardiac type. The temperature is lower. While in general the valvular disease retards the tuberculous processes, this is not always true, and the case may advance with extreme rapidity, the hemorrhage may be dangerously severe, and the lung condition may aggravate the heart disease. Anders found these cases unsuitable for mountain sanatoria.

Although a lesion at the mitral valve is associated with a relative exemption from phthisis, quite an opposite condition is met with in patients suffering with a lesion at the pulmonic orifice. This was recognized by Lebert, who reported 25 cases in which tuberculosis followed a primary disease of the pulmonary valve. Rokitansky took this finding as support for his hypothesis, holding that in pulmonary stenosis the supply of blood to the lungs was decreased, hence there was a greater susceptibility to phthisis.

Lebert estimates that 33 per cent of cases of pulmonary stenosis die of consumption if they live to their 20th year. Stoelker reported 16 cases of congenital pulmonary stenosis, and concluded that 14 per cent of all such cases living to the age of 20 die of pulmonary tuberculosis. In 5 out of 6 cases reported by Shultz there was consumption. Anders reviews the literature relating to tuberculosis with pulmonary stenosis and gives references to 36 cases.

II.

Endocarditis Arising in the Course of the Tuberculosis but not Produced by the Bacillus Tuberculosis.

A. We may make mention here of that large group of cases showing at autopsy a healed or latent focus of tuberculosis. Probably the great majority of all endocarditis cases present some tuberculous lesion. In most cases dying of endocarditis, in whom there is no clinical sign nor symptom of tuberculosis, a careful search at autopsy will reveal an old tuberculous scar or a focus of latent tuberculosis. Such a focus is found in a large percentage of all autopsies, the number varying with the observer, with the age of the patients, and with the locality. In general the percentage ranges from 40 to 80 per cent, although Naegeli claims that careful search will reveal such a focus in 100 per cent of all those who have reached 18 years. It is to be expected, therefore, that this group will furnish the largest number of cases in which tuberculosis and endocarditis are found together. In this connection it may be noted that the period of life at which the largest proportion of tuberculous patients is found, overlaps the age for the maximum incidence of acute rheumatism and endocarditis. These cases are of no clinical importance.

I can find no literature referring to latent tuberculosis in endocarditis. In the routine autopsies at this hospital no special effort is made to find a latent focus of tuberculosis, and in looking over the autopsies on endocarditis patients I have found only 20 such cases. 12 times the focus was in the lung; 3 times in the pleura; 3 times in a lymph gland; once in the pericardium; once a general serous tuberculosis. The condition was not recognized clinically in any case.

Reference may be made incidentally to another relationship between endocarditis and tuberculosis. Not infrequently an obscure case is met with in which these conditions may be confused. I found one case among the medical histories in which a diagnosis of tuberculosis was made clinically, while at autopsy this did not exist but an endocarditis was discovered.

B. In a number of cases a tuberculous patient receives a valvular infection from a secondary bacterial invasion. This secondary infection may occur either at the area of tuberculous infection, or the bacteria may find another portal of entry.

As we have seen, acute endocarditis is found in about 5 per cent of phthisical patients, but it seems probable that only a small proportion of these endocarditides are caused by the B. tuberculosis, the greater number being caused by other bacteria. Although many cases of endocarditis in tuberculosis have been described, there are very few in which it is clear that the endocarditis is a tuberculous process. The difficulties in the way of establishing the nature of an endocarditis will be discussed presently. We may say, however, that endocarditis not obviously of a tuberculous nature must be looked upon as at least doubtful, and such cases can be considered conveniently in this group of non-tuberculous endocarditides.

Most of the cases in the literature are of this character. Two groups of cases are to be considered here, those in which the bacteriology of the vegetation is unknown, or non-tuberculous, and those in which the tubercle bacilli occur but are not proven to be the cause of the endocarditis.

a. The tricuspid endocarditis described by Lancereaux (1866), quoted by Banquet, is not definite enough to enable us to make a diagnosis of the nature of the process. The same may be said of Letulle's (1875) description of the small vegetations forming a thick fringe on the valves of children who died of acute general miliary tuberculosis with signs of valvular (aortic) insufficiency.

Percy Kidd (1887) could not demonstrate tubercle bacilli

in sections from his series of cases, nor could he find good reason to believe that the endocarditis was due to this bacillus.

In the case reported by Griode (1889), quoted by Banquet, the very large fleshy vegetations on the tricuspid valve and in the right auricle showed no tubercle bacilli on stained section nor in culture. Bernheim's case of tricuspid endocarditis extending up over the endocardium of the auricle (see Banquet) was similar. In the same group we may include Osler's series, which were considered by him to be non-tuberculous.

The following cases also are to be included in this group: Potain's cases; the four cases of Hanot (1893); three out of Etienne's series of five (Nos. 3, 4, and 5); at least six and possibly seven of Harbitz's series of nine; most if not all of Teissier's series of 42 cases (cited by Anders). In only 12 of these cases were tubercle bacilli found on the vegetations. In one of v. Leyden's cases the vegetation showed streptococci.

b. Tubercle bacilli in endocardial vegetations.

Kundradt, Heller, and Cornil, working independently, demonstrated tubercle bacilli in endocardial vegetations in 1886. While this finding furnishes some evidence that the bacillus is causing the endocarditis, the objection has been raised that the bacteria may have been deposited by accident from the circulation upon an already existing vegetation, or may be contaminations due to technique. In order to establish the causal relationship between the tubercle bacillus and a vegetation, the bacillus must be present not only on the surface but in the deeper part of the vegetation, and must produce some anatomical alterations that are characteristic. In the following cases the tubercle bacilli were found either in stained sections of the vegetation, in cultures, or by inoculation of guinea-pigs, but whether their occurrence was accidental or whether the vegetation was a true tuberculous process cannot be definitely determined.

In two of Etienne's cases (1898) the tubercle bacillus was found by inoculation of guinea-pigs. Rindfleisch's and Buskart's cases are apparently of this group (mentioned by Londe et Petit).

Harbitz found the tubercle bacillus in 2 of his 9 cases, but considered their presence accidental. Judging from his histological description, one of the cases may well have been a true tuberculous endocarditis.

III.

The cases of endocarditis resulting either directly or indirectly from the action of tubercle bacilli may be grouped under several headings as: 1. Miliary tuberculosis. 2. True tuberculous endocarditis. 3. Tuberculous cardiac thrombi. 4. Tuberculous endocarditis from extension of a myocardial tuberculosis. 5. Toxic endocarditis of tuberculous origin.

1. Miliary Tuberculosis.

Although Corvisart, in 1806, described tubercles on the mitral valve, and Townsend, in 1832, described a large solitary tubercle one inch in diameter in the wall of the left auricle which apparently caused death from asphyxiation, the opinion prevailed generally that tuberculosis does not attack the wall of the heart nor blood-vessels. In 1859 v. Recklinghausen reported miliary tubercles under the endocardium of the auricle and ventricle of a patient who had died of chronic tuberculosis with miliary tuberculosis. The tubercles were translucent or opaque, projected slightly above the level of the endocardium, and also into the myocardium, and were covered with a smooth layer of endocardium. He considered that they started from the layer of myocardium just next to the endocardium.

In 1874 Letulle described what were probably miliary tubercles in the wall of the left ventricle of a five months' old infant dead of general miliary tuberculosis.

In 1878 Sänger reported two cases—a 9 months' old infant and a boy 7 years old,—and reviewed the literature of tuberculosis of the heart.

The study of tuberculosis in the endocardium assumed a special interest after the classical work of Weigert, 1878-82, demonstrating the mode of origin of acute general miliary tuberculosis, in which he showed that this disease depends upon a primary vascular focus of tuberculosis for its origin and spread. In two of the cases of miliary tuberculosis which he reported, both of them with a tuberculous thrombus in the pulmonary vein, he found "in the conus arteriosus dexter a few gray nodules projecting above the endocardium." The nodules were from pin-point to pin-head size. He said: "Miliary tuberculosis of the heart belongs to the *almost* regular occurrences in acute general miliary tuberculosis. It is probably absent once in ten times. The seat of preference is the conus arteriosus dexter, as far as the large papillary muscle inclusive, where the tubercles occur most regularly as fine, gray, or whitish nodules on the endocardium, which is appreciably raised over them. Second in order of frequency comes the endocardium of the right ventricle in general, then that of the left, especially on the septum." All subsequent observers have verified these findings of Weigert.

Benda calls attention to the fact that these are not endocardial but are really myocardial tubercles, as v. Recklinghausen described them, and lie beneath the elastic coat of the endocardium. They cannot be considered examples of true endocardial tuberculosis, unless they have ulcerated into the cavity of the heart, or unless an elastic tissue stain shows that the tubercle is above the elastica of the endocardium. Benda has reported such a case, which at autopsy was identical with the usual subendocardial tubercles. The cases of G. Lyon, Tiry, and Auché and Chambrelent, described by Banquet as true endocarditis, were probably subendocardial tubercles.

2. True Tuberculous Endocarditis.

v. Leyden includes the cases of Kundradt and Heller in this class, although Heller's case probably belongs to the group just considered. Tripier reported a case in 1890 presenting a mitral endocarditis in miliary tuberculosis. The nodule on the under face of the valve looked like a tubercle, and in stained sections showed appearances similar to those

seen in a tubercle, with giant cells, embryonal cells, a break in the elastica, and direct connection with the heart cavity. The valve was thickened. The cellular infiltration of the valve increased progressively from the base of the valve to the vegetation. Benda considers this the first case in which the connection between the endocarditis and the tubercle bacillus is definitely established. Birch-Hirschfeld described a vegetative and ulcerative endocarditis (1891) with tubercles, giant cells, etc., on the valves. Londe et Petit (1894) found a few tubercle bacilli in the vegetation, with a rather suggestive histological picture, and produced tuberculosis in a guinea-pig by inoculation. Although they did not consider their case a tuberculous endocarditis, and ranked it as undetermined, it seems fair to consider this a true tuberculous endocarditis.

v. Leyden (1896) reported upon endocarditis in tuberculosis. In his four positive cases the tubercle bacilli were found not simply on the surface but all through the vegetation, often many within one cell. In one case the diagnosis was made clinically of endocarditis, probably tuberculous. He was of the opinion that the bacteria were carried to the endocardium inside of cells.

In two of Etienne's cases (reviewed by Banquet) the fresh vegetations were carefully washed in sterile water to remove any bacilli from their surfaces, and inoculated into guinea-pigs in which tuberculosis developed.

In 1899 Benda reported two cases, which he ranks in his review of the subject as being, with Tripier's case, the only authentic cases of tuberculous endocarditis. His description, however, is not convincing.

Michaelis and Sanford Blum injured the aortic valves of rabbits, injected tubercle bacilli and produced a typical verrucose endocarditis with numerous tubercle bacilli in the vegetations and no other bacteria.

3. Tuberculous Cardiac Thrombi.

These thrombi, first described by Rokitansky (according to v. Leyden), were carefully considered by Birch-Hirschfeld in 1891 (Versammlung Deutscher Naturforscher and Aerzte, September 24, 1891). In the right auricular appendage of his case was a thick, fibrous, fleshy, adherent body, at first taken for sarcoma but under the microscope found to be a tuberculous thrombus, showing masses of leucocytes, areas of organization, caseous foci, and foci of recent typical tuberculosis, the latter usually in the depth of the thrombus, but also occasionally near the surface. Hirschsprung's case (1882) is, according to Benda's view, the first case of this kind that was reported. Whether Townsend's case (1832) was a solitary tubercle of the myocardium or a tuberculous cardiac thrombus is not certain, though apparently it was myocardial. Leuken's case is also not very definite (1865). This condition has been described also by Weichselbaum, Klebs, Kotlar, Chiari (see Nothnagel), and by Pick and Cade.

4. Tuberculous Endocarditis from Extension of a Myocardial Tubercle into Endocardium.

Moser, in a case of phthisis and tuberculous epididymitis, found an organizing thrombus containing caseous areas, giant cells, and tubercle bacilli. The endocardium was replaced by a rather thick layer of fibrous tissue on which the thrombus rested. He thought the process started beneath the endocardium and extended into the endocardium and thrombus.

In 1902 Sternberg demonstrated a specimen of a tubercle 2 to 3 inches in diameter in the wall of the right auricle which had ulcerated into the auricle and produced a general miliary tuberculosis. Cases such as these of Moser and Sternberg are not numerous. In this connection an article by Cabannes may be noted. In this he analyses 53 cases of tuberculosis of the myocardium. In 8 of these the auricle alone was affected, in 12 it was affected chiefly, the right auricle more than the left. The disease usually occurs as a solitary tubercle, in most cases arising from a pericarditis. These myocardial tubercles, however, give rise to tuberculous thrombi and tuberculous ulcers in the endocardium only in rare instances. Benda, in his review, gives as the only authentic examples of this form of tuberculous endocarditis the cases of Leuken (1865), Schürhoff, and v. Genersich.

5. From this review it is evident that it is no easy matter to prove that any given endocardial vegetation is produced by the tubercle bacillus. The bacilli must be demonstrated not on the surface but in the depth of the vegetation, where their presence could not be due to accidental contamination, and in this search stained sections are of more value than cultures or inoculations, as the position in which the bacteria occur is more certainly determined by this method. It must be shown by staining sections that the bacilli have not simply lodged in the vegetation but are actually associated with the lesions typical of tuberculosis, and finally, as Benda emphasizes, the elastic tissue stain must be employed to prove that the process is above the elastica, that is, in the endocardium, and not below, that is, in the myocardium. As we have seen, such complete proof has been furnished in few cases, and some writers, particularly the French, hold that the endocarditis in tuberculosis is due not to the direct activity of the bacilli in the vegetation, but to a toxin elaborated by the bacilli elsewhere, and carried by the circulation to the valves, where a toxic endocarditis is produced. Teissier, Hanot, Potain, and others are advocates of this view, Teissier holding that 40 per cent of cases show sclerotic changes in the valves. While sclerosis of the valves may result from the toxic materials circulating in tuberculous patients, just as we find a similar process after typhoid, it seems hardly probable that the vegetations arise from the toxins in the circulation alone. The bacilli in a vegetation may be missed for several reasons. A few bacilli lodging in the endocardium may furnish a focus of injury upon which a relatively large thrombus develops, all except the starting point of the thrombus being a bland propagated thrombus. It would only be by studying serial sections that the tuberculous focus would be found in such a case. Furthermore, the bacteria may be of low vitality, and may die out in the vegetation. In other cases of endocarditis now being studied a number of cases are found in which

cultures from the vegetations were sterile, or the cultures died in the tubes very rapidly, while sections through the vegetation showed traces of degenerated cocci, which had evidently given rise to the disease. Death of the bacteria in this situation would be especially apt to occur if the body forms any protective substances harmful to the parasite, for the vegetations are constantly bathed by a large volume of fluid in which the protective substances are carried, and are in a position favorable for attack by phagocytes.

The following cases were found in a review of the medical and pathological records of the cases of endocarditis treated at the Johns Hopkins Hospital.

Endocarditis Preceding Tuberculosis.

Autopsy 88.—Th. W., white, female, admitted February 26, 1890. Illness began about 8 months before with a profuse hemorrhage, after which patient was well until three months ago. At that time cough, with expectoration began, and patient began to lose weight and became dyspnœic.

Clinically the patient had tuberculous cavities in the lungs, bacilli in the sputum, and a systolic murmur at the apex of the heart.

At autopsy, in addition to tuberculosis of the lungs with cavities, and ulcers in intestine, there was an acute and chronic endocarditis of aortic and mitral valves.

In this case the chronic process probably preceded the tuberculosis.

Autopsy 276.—W. B., age 23, white, admitted January 21, 1892. Illness began less than 9 weeks before death with tuberculosis; when seen at hospital, in addition to signs of phthisis, he had a systolic murmur at apex and an accentuated pulmonic second; at autopsy, a chronic mitral endocarditis with insufficiency and stenosis, caseous bronchopneumonia and acute general miliary tuberculosis.

Miliary Tubercles in Endocardium.

Autopsy 8.—In a case showing chronic tuberculous pericarditis, acute general miliary tuberculosis, and chronic thickening of the aortic and mitral valves, "numerous very small gray miliary tubercles were found beneath the endocardium of the right auricle near the entrance of the superior vena cava."

Autopsy 415.—With chronic productive pleuritis with many tuberculous abscesses and acute general miliary tuberculosis, there was found on one leaflet of the mitral valve midway between the margin and base of valve, a distinct yellowish-white miliary tubercle.

Autopsy 633.—In an infant 11 months old, with rickets and tuberculous cervical and thoracic glands, there arose a caseous pneumonia and miliary tuberculosis, with 2 or 3 tubercles beneath the endocardium.

Autopsy 654.—A child of 3 years, with tuberculous glands and general tuberculosis, showed one nodule, apparently a miliary tubercle, at the base of the mitral valve.

Autopsy 783.—D. I., 45 years, black. Chronic peritoneal tuberculosis and acute general miliary tuberculosis, several subendocardial miliary tubercles appearing in right auricle, together with subepicardial and myocardial tubercles.

Non-Tuberculous Endocarditis in Tuberculosis.

Autopsy 41.—S. D., 19 years, black, female. Clinical course of rapid tuberculosis; no hemorrhage and persistent high fever. At autopsy, in addition to cavities in the lungs, etc., were found fresh soft granulations on the mitral valve.

Autopsy 427.—C. M., 40 years, white, female. The clinical course was obscure, no definite signs at heart or lung, but a high, irregular, septic temperature. At autopsy pulmonary tuberculosis with cavities was found associated with acute general miliary tuberculosis and an ulcerative endocarditis of the mitral valve. No tubercle bacilli were found in the valve ulcer.

Autopsy 783.—J. J., 36 years, white, male. The case presented clinically the signs of adherent pericardium and cardiac insufficiency. At autopsy, tuberculous adhesive pericarditis, etc., and subacute endocarditis of aortic, mitral, and tricuspid valves.

Autopsy 1874.—Wm. Mac. P., 48 years, black. Was treated for diabetes mellitus, the heart and lungs showing no characteristic changes. At autopsy, a cavity with tuberculous bronchopneumonia was found and acute endocarditis of the aortic and mitral valves with vegetations on the wall of the left auricle.

Autopsy 1131.—G. W., 58 years, black, male. Clinically, this case was diagnosed as tuberculous peritonitis, which was found at autopsy, together with a tricuspid ulceration.

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A CASE OF ACQUIRED CYST OF THE CONJUNCTIVA CONTAINING AN EMBRYONIC TOOTHLIKE STRUCTURE.[1]

By Edward Stieren, M. D., *Pittsburg, Pa.*

The following case of embryonic osseous tissue forming in the conjunctiva is unique in that it developed after the tenth year of life.

The patient, Miss M., aged 16, was brought to me by her cousin, Dr. Paul J. McLain, on account of a tumor of the left eye ball. The history of the case, as recited by her mother, is as follows:

The growth was first noticed when the patient was ten years of age. (The parent is positive that no growth was present during infancy.) At that time the tumor was about the size of a pin-head. From ten years of age until two and one-half years ago it increased very little in size and gave no trouble whatever. The child then began to complain that the growth annoyed her; there was no pain, simply a disagreeable feeling. From this time the tumor began to increase in size rapidly. During the last six months it annoyed her considerably, causing almost constant headache.

Examination.—With the patient looking downward and inward by retracting the upper lid one could see a tumor of the bulbar conjunctiva. The growth has every appearance of a dermoid cyst of the conjunctiva, is about the size and shape of an ordinary navy bean, and can be made to move slightly in all directions by force applied with the lid margin.

Excision was advised, and under holocain and adrenalin local anæsthesia the tumor was grasped with a blunt-tooth forceps. The sensation of a foreign body was imparted to the touch through the forceps, suggesting calcareous degeneration of the cyst. The tumor had rather a firm attachment to the episcleral tissue, but was shaved off with a cataract knife without difficulty. A small quantity of straw-colored fluid escaped from the cyst, the cavity being almost entirely filled with what appeared to be a well formed, beautifully white, incisor tooth. It possessed a covering, no doubt periosteum, very loosely attached, which was, unfortunately, lost in making a dry preparation of the specimen. The "tooth" had a well defined crown and neck with a tapering extremity resembling a fang. It measured 15 mm. in length, 9 mm. in its widest diameter, with an average thickness of 2 mm. Half of the structure was prepared as a dry specimen and the other half given to Dr. Elizabeth Moore, pathologist at Passavant Hospital, for histological study.

Histological Examination.

The portion of the specimen used for histological examination was decalcified slowly in 1 per cent. hydrochloric acid solution. After decalcification, the usual technique of making celloidin sections was employed. Cross sections were made which were stained in hæmatoxylin and eosin and in indigo-carmine. The microscopical examination reveals a well developed bone formation. The section presents a curved and a straight margin. On the curved margin the lamellæ are parallel to the external surface of the specimen and, probably, correspond to the fundamental lamellæ of true bone. The parallel system occupies about one-third the transverse diameter of the section. Scattered between the lamellæ are the spaces known as lacunæ—the bone corpuscles. The spider-like processes by means of which the lacunæ communicate—the canaliculi—can be easily seen. The remainder of the section is occupied by distinct Haversian systems. About each Haversian canal are the concentric lamellæ, with the lacunæ communicating by their canaliculi with the canals. In many places the Haversian canals show an endothelial lining. Between the Haversian system are lamellæ which correspond, probably, to the interstitial lamellæ of normal bone. The parallel system blends with the Haversian system at the ends of the section. By the indigo-carmine stain a few of Sharpey's fibers between the lamellæ can be demonstrated.

[1] Read at the annual meeting of the American Ophthalmological Society. May 11, 1905.

Since the foregoing was written I have been informed by Dr. Edward Jackson that a similar condition was reported by Galtier, under the title "Subconjunctival Osteoma," in the *Annales d'Oculistique*, March, 1895, the article being abstracted in the *Ophthalmic Review* for May, 1895. Through the kindness of Dr. Myles Standish I was able to refer to the original article this morning. The author says, in part: "Occurrences of this nature are very rare. No mention is made of them in the best known works upon the pathology of the eye, and it is only in the extensive treatise by de Wecker and Landolt that we find a short chapter upon this subject. Three cases are therein noted: one by von Graefe, one by Saemisch, and one by de Wecker."

Galtier reports a case of a girl ten years of age occurring in his practice. When the right eye, turned downward and inward, a well defined projection the size and form of a slightly flattened pea was found at the equator of the eye, above the horizonal meridian and behind the equator. The growth was removed with toothed forceps and scissors. The author states: "What was my surprise, upon dissecting it, to find its contents hard, absolutely osseous, and formed of very compact tissue." Its length was one centimeter, its breadth, seven millimeters. The question that occurred to the author was whether this was really a new growth, or a portion of normal bone accidentally detached from one of the orbital walls. An histological examination showed that the bony tumor appeared to be composed of normal osseous tissue. The author's suggestion that the growth might be due to the presence of a fragment of detached bone rather than to an actual neoplasm, is supported by the history that the child had received a blow by falling and striking the right side of her face and forehead some six or seven months before. At the time, however, there was nothing which pointed to injury of the eye, and as his case resembles very closely the three recorded in de Wecker and Landolt's work, and the one reported by myself, and there is no history of traumatism in any of the four, I give his theory very little weight. It seems to have made a deep impression in Galtier's mind, however, as he concludes his article by saying: "I even question whether the subject of sub-conjunctival osteoma is a legitimate one, and whether the cases quoted would not better be included under the head of fractures of the orbital vault, with an encysted movable fragment of bone; this classification would slightly alter the prognosis, although it is true that these



tumors are, up to the present time, classed with benign tumors of the conjunctiva."

In the histological examination of the case reported by me, it will be remembered that in several instances the section showed embryonic bone tissue, thus proving conclusively that bone can develop in the conjunctiva. Hence, it appears to me that Galtier's hypothesis in regard to osteomata, being encysted fragments of bone detached from the surrounding bony parts, is based on very slender facts indeed.

SOME OBSERVATIONS ON THE OCCURRENCE OF MICROCOCCUS ZYMOGENES.

By E. G. Birge.

[*From the Pathological Laboratory of the Johns Hopkins Hospital, Baltimore.*]

In the Journal of Experimental Medicine for 1899, MacCallum and Hastings described a new micrococcus, named by them *Micrococcus zymogenes*, which they isolated from a case of vegetative endocarditis both from the circulating blood and at autopsy. The micrococcus thus isolated was pathogenic for most of the ordinary laboratory animals, the animals dying of a general septicemia or, in some cases, of an acute endocarditis.

Since then Harris and Longcope have reported five more instances of the occurrence of the organism; in one case from a cesspool in Baltimore, and in the remaining four cases it was found as a secondary invader at autopsies in the Johns Hopkins Hospital. In two of these cases the organism was entirely non-pathogenic; in the other three it was only slightly pathogenic for the ordinary laboratory animals.

While working upon the bodies of certain crows sent to me from Washington I isolated an organism resembling that described by MacCallum and Hastings, but differing in some

respects from their organism. There were no lesions which could be attributed to the organism. It was isolated from the mucous exudate in the larynx in all cases.

Description of the Microorganism.

Morphology.—Stained preparations show the organism to be a micrococcus either spherical or very slightly oval in shape. It occurs singly, in clumps, and in a few preparations from bouillon cultures in chains of six to eight individuals, although in hanging-drop preparations a few chains of sixteen organisms were noted. The most frequent form of occurrence, however, is in pairs.

Hanging-drop preparations show the organism to be non-motile.

It stains well with the ordinary aniline dyes and remains deeply stained by Gram's method. Attempts to demonstrate capsules or spores by the various methods of staining were negative.

In size the organism is very much smaller than the *Micrococcus lanceolatus.*

Cultural Characteristics.

Agar.—Cultures made on agar slants gave at four hours a barely perceptible growth of discrete pin-point, grayish-white colonies. At twenty-four hours the growth was profuse, flat, slightly elevated, and restricted to the path of the needle. The growth by reflected light is of a grayish-white color; by transmitted light is translucent and of a smoky-brown color, seen best in old cultures.

The edges of the growth are usually somewhat serrated and elevated by the growth of larger colonies, sometimes discrete.

Colonies.—The discrete colonies on agar are very small, seldom exceeding one millimeter in diameter. Their characteristics are the same as noted above.

Ascitic agar.—The growth was the same as on nutrient agar, but was much more profuse.

Litmus glucose agar.—Stab cultures in litmus glucose agar gave a production of acid but not of gas. The acidity was distinctly noticeable along the line of the stab after four hours.

Bouillon.—Cultures in bouillon showed, after four hours, a slightly diffuse cloudiness, more profuse at twenty-four hours with no sediment. In the course of several days the organisms settled to the bottom of the tube, leaving the overlying fluid clear. No indol was produced either in bouillon or Dunham's solution.

Potato.—The first few cultures on potato showed no growth. After several generations there was a moderate growth; small colonies appear first after about 36 hours, later they become confluent. The growth is slightly elevated and somewhat moist at first. Later it becomes dry and brownish.

Gelatine.—A somewhat grayish, granular and opaque growth appears along the path of the needle in stab cultures in gelatine. In forty-eight hours a slight cupping of liquefaction appears at the surface, extends slowly downward, and eventually involves the whole medium. The liquefaction is much slower than in the case of the *Staphylococci.*

On gelatine plates small, pin-point, granular colonies appear, yellowish by transmitted light, which float in a cup of liquefied gelatine.

Blood serum.—The growth on blood serum resembles that on plain nutrient agar, but is more profuse. The surface of the medium at twenty-four hours is very moist, and in the course of several days the blood serum is partially liquefied. The fluid is clear and the solid medium is broken down.

Milk.—The most characteristic cultural reactions appear in its growth on milk. In litmus milk at four hours the litmus is completely decolorized, except for a narrow purplish band at the top, without coagulation of the milk. On shaking the culture the color returns throughout the medium but is lighter and a trifle more reddish than the original culture. This decolorization of the litmus is evidently due to deoxidation.

At twenty-four hours the medium is decolorized with a narrow purplish-red ring around the top as at four hours. On shaking, the color returns throughout the medium but is distinctly redder than before. There was a slight coagulation of the medium at twenty-four hours, which became very firm at thirty hours. The upper layers became softened and changed into a clear fluid definitely red at the surface, straw-colored below. This softening and liquefaction of the coagulum continued until there is a clear fluid throughout with a flocculent deposit at the bottom, the remains of the coagulum. The red color extends deeper into the fluid, and finally extends throughout the deposit, leaving ultimately a clear straw-colored supernatant fluid lying over the deep red deposit.

These reactions in litmus milk are absolutely constant, and when the organism isolated by MacCallum and Hastings was used as a control the changes followed one another in both cultures practically identically in time.

Pathogenesis.—Rabbits and pigeons were inoculated in various ways with suspensions of the organism. In all cases the result was negative.

One rabbit was inoculated intravenously with 2.5 cc. of a thick bouillon suspension from an agar culture, and ten days later it received 3 cc. of a similar suspension. After the first inoculation the rabbit was evidently sick for a day or so, but no reaction followed the second inoculation. Four days after receiving the second inoculation the animal was killed and the organism was recovered from the liver in pure culture. Cultures were also made from the heart's blood and spleen but remained sterile. There were no lesions in any of the organs. A second rabbit was inoculated intravenously with 2.5 cc. of a bouillon suspension of a similar twenty-four hour culture, but showed no reaction. A pigeon inoculated subcutaneously into the breast with a bouillon suspension of a twenty-four hour culture of the organism, recovered from the liver, showed no reaction whatever, either locally at the site of inoculation or generally.

Another pigeon inoculated subcutaneously with 2 cc. of a

bouillon suspension of the original organism gave a negative result.

These results are at a variance with those of MacCallum and Hastings, their organism being very pathogenic for all ordinary laboratory animals except guinea-pigs, white rats, and pigeons, which showed little susceptibility to inoculation.

In order to prove this organism to be identical with that of MacCallum and Hastings, a rabbit was immunized against it by intravenous injections of the organism in increasing amounts. Serum dilutions of 1:50 were made with suspensions of both organisms. There was a complete agglutination in both cases within two hours. The agglutination test was made macroscopically.

Ferments.—A culture in milk in which the process of liquefaction was going on was filtered through a Berkefeld filter, and about .5 per cent of carbolic acid was added to the filtrate to prevent the possible growth of any organism. A small quantity of this filtrate was added to sterile tubes of litmus milk. After thirty-six hours there was a soft coagulum which later contracted, leaving in the upper part of the tube a clear supernatant liquid. The process was similar to that set up by the live organisms, but was very much slower, and there was practically no change in the reaction of the milk.

Cultures and stained preparation, made from the filtrate and the milk, showed no organisms.

Summary.

From the mucous exudate in the larynx of certain crows a micrococcus was isolated, corresponding morphologically and culturally with that isolated by MacCallum and Hastings from a case of vegetative endocarditis.

The organism, however, was not pathogenic for any of the ordinary laboratory animals, large doses having at the most a very slight effect.

A rennin-like ferment is secreted by the organism, which does not appear to be affected by small amounts of carbolic acid.

The organism can be distinguished from *Streptococcus pyogenes* on one hand, and on the other from the *Staphylococci*, by its characteristic cultural reaction in milk and by its doubtful pathogenicity.

I wish to acknowledge my thanks to Mr. W. J. Bennet, of Washington, D. C., for the material with which the work was done.

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NOTES ON NEW BOOKS.

The Surgical Diseases of the Genito-Urinary Tract. Venereal and Sexual Diseases. A Text-Book for Students and Practitioners. By G. Frank Lydston, M. D. (*Philadelphia: F. A. Davis & Company, 1904.*)

Dr. Lydston's book has already taken a place among the more useful works on this subject, and those who have profited by the first edition will welcome the second with its additions and improvements. The work is a fairly satisfactory one for students; it contains the chief facts of this branch of medicine and surgery, and they are as a rule set down without undue expansion. One might be justified, in these days, in criticising unfavorably the rather crude illustrations found throughout the book. The drawings, for instance, which represent the introduction of a catheter teach no more than the fine photographs of the same procedure in White & Martin's text-book, and as works of art they are little short of barbarous. The author has elected to close his volume with a complete list of his own publications on genito-urinary subjects; one wonders if the author's photograph as a frontispiece would not have made a most fitting companion piece.

A System of Practical Surgery. By Prof. E. von Bergmann, M. D., Prof. P. von Bruns, M. D., and Prof. J. von Mikulicz, M. D. Volume V. Surgery of the Pelvis and Genito-Urinary Organs. Translated by William T. Bull, M. D., Columbia University, New York. (*New York and Philadelphia: Lea Bros. & Co., 1904.*)

This volume impresses one as a most uneven performance. The chapter by Schede on the surgery of the kidney and ureter leaves little to be desired; but the bladder and prostate have hardly had justice done them by the father of cystoscopy. An important feature in the actual handling of cases, often overlooked in conventional text-books, is here thoroughly treated, and the student who wants to know what happens (or should happen) to patients when they leave the amphitheater where he has seen them operated upon, will get some satisfaction in this discussion of after-treatment. Palliative treatment, too, receives the consideration which it ought to get in a text-book of surgery, but which it usually has to forego.

Certain opinions rather dogmatically expressed run counter to American, or at least to Baltimorean, ideas, and from this point of view invite attention. The best method of treatment of prostatic hypertrophy is said to be the regular use of the catheter—an opinion expressed and sustained with what appears to be a fine disregard of all the recent work on the subject, and with no proviso as to the class of cases in which such a method of treatment is manifestly unwise. The prognosis of urinary fistulæ is said to be good, no mention being made of the large class of cases in which it is notoriously bad. The determination of the quantity of urea in the urine is said to be a procedure quickly and easily carried out, a dogma hardly sustained by recent work. Opium is said not to be necessary after anal operations, and yet it is advised that, after the Whitehead operation, the bowels be kept confined for eight or ten days. One wonders if, after such a long period of quiet, it would be worth while starting them again at all in elderly patients.

The chapter on cystoscopy is most elementary, only the very grossest description of the things seen being given. Other incomplete treatments and omissions include an absence of any mention of the abdominal incision for varicocele operations, the suave neglect of the large subject of perineal prostatectomy, the cursory discussion of the suprapubic route, and the failure to mention, or at last to emphasize, pollakiuria—the most important and often the earliest symptom of prostatic hypertrophy.

As to the fortune which has fallen to the German edition in

preparing it for American readers, an occasional ill-chosen adjective, a gauche expression here and there, and frequently recurring typographical errors (see p. 558, where "catheterize" and "cauterize" are hopelessly mixed) leave the impression that the work has not been done with nice attention to detail.

Travaux de Chirurgie. Anatomo-Clinique. Par HENRI HARTMANN. (*Paris: Georges Steinheil, 1904.*)

This volume, for which the versatile Hartmann makes himself responsible, contains the reports of work done at L'Hopital Lariboisiére and elsewhere on the surgery of the urinary tract and testicles. It includes an exhaustive article on the solid tumors of the kidney and a more or less trivial one on the bacteriology of acute vaginalitis; it corresponds more closely to an American Hospital Report than to a text-book, and should not, therefore, be criticized for lack of structure—an attribute which we could justly demand of a "book." On the average, the high standard of Parisian urology is maintained and the articles are for the most part thorough and painstaking. It cannot be said that the collection represents any noteworthy addition to surgical knowledge.

Errors of Refraction and Their Treatment: A Clinical Pocket-Book for Practitioners and Students. By CHARLES BLAIR, M. D., Fellow of the Royal College of Surgeons of England. (*Bristol: John Wright & Co.; London: Simpkin, Marshall, Hamilton, Kent & Co., Ltd., 1905.*)

This is a small book of 100 pages on the first principles of refraction. As all text-books on the eye, large and small, contain as much, if not more, matter on refraction, we hardly see what sphere this book aims to fill. The book is too elementary and too much abbreviated to be of service to anyone who wishes to seriously take up the study of the refraction errors of the eye and their correction with glasses. B. B. B., JR.

International Clinics. A quarterly of Illustrated Clinical Lectures and especially prepared Original Articles on Treatment, Medicine and Surgery, etc. Vol. IV, Fourteenth Series; Vol. I, Fifteenth Series. Edited by A. O. KELLY, A. M., M. D. (*Philadelphia: J. B. Lippincott Co., 1905.*)

A systematic review of even the ablest articles in these two volumes is out of the question. In them is to be found the usual subjects of interest in each special branch of the profession. Some are excellent, many full of important data.

Weber and Watson report a case of chronic polycythæmia with enlarged spleen (Vaquez disease), and bring forward evidence to show that the increased production of erythrocytes occurred in the bone-marrow, which has been stimulated by circulatory disturbances in some cases, and in others by a "primary excessive vital reaction."

Duckworth in another paper points out that, contrary to his former opinion, gouty ailments, at least in the larger cities of America, occur not infrequently, though usually in the so-called "incomplete forms."

In Volume I of the present series there are three interesting papers on the diagnosis of cardiac disease, as well as a paper on "Skin Grafting in the Late Treatment of Severe Burns," which merit a perusal. Here one also finds a very careful resumé of the progress of medicine and surgery by Stevens, Esdall, and Bloodgood. C. P. H.

BOOKS RECEIVED.

A Manual of Practical Hygiene. For Students, Physicians, and Medical Officers. By Charles Harrington, M. D. Third edition, revised and enlarged. Illustrated with twelve plates in colors and monochrome, and one hundred and eighteen engravings. 1905. 8vo. 793 pages. Lea Brothers & Co., Philadelphia and New York.

A Nurse's Guide for the Operating Room. Second edition, enlarged and revised. By Nicholas Senn, M. D., Ph. D., LL. D., C. M. Published under the direction of the Sisters of Charity, St. Joseph's Hospital, Chicago. [1905.] 8vo. 204 pages. W. T. Keener & Co., Chicago.

A Practical Treatise on Fractures and Dislocations. By Lewis A. Stimson, B. A., M. D., LL. D. (Yalen). Fourth edition, revised and enlarged. With 331 illustrations and 46 plates in monotint. 1905. 8vo. 844 pages. Lea Brothers & Company, New York and Philadelphia.

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A Text-Book of Medical Chemistry and Toxicology. By James W. Holland, A. M., M. D. Fully illustrated. 1905. 8vo. 592 pages. W. B. Saunders & Company, Philadelphia and London.

A Text-Book of Obstetrics. By Adam H. Wright. With two hundred and twenty-four illustrations in the text. 1905. 8vo. 591 pages. D. Appleton & Company, New York and London.

A Text-Book of the Practice of Medicine. By Hobart Amory Hare, M. D., B. Sc. Illustrated with 129 engravings and 10 plates in colors and monochrome. 1905. 8vo. 1119 pages. Lea Brothers & Company, Philadelphia and New York.

Acute Contagious Diseases. By William M. Welch, M. D. and Jay F. Schamberg, A. B., M. D. Illustrated with 109 engravings and 61 full-page plates. 1905. 8vo. 781 pages. Lea Brothers & Co., Philadelphia and New York.

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VOLUME I. 423 pages, 99 plates.

VOLUME II. 570 pages, with 28 plates and figures.

VOLUME III. 766 pages, with 69 plates and figures.

VOLUME IV. 504 pages, 33 charts and illustrations.

Report on Typhoid Fever.

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CONTENTS.

	PAGE
The Early Diagnosis and Radical Cure of Carcinoma of the Prostate. Being a Study of 40 Cases and Presentation of a Radical Operation which was Carried Out in Four Cases. By Hugh H. Young, M. D,	315
Action of the Toxic Agent of Lobar Pneumonia: Therapeutics. By Walter V. Brem, Jr., M. D.,	321
A Case of Unusually Large Aortic Aneurysm. By Wm. H. Hough, M. D.,	331
Acute Pericarditis Complicating Acute Lobar Pneumonia. By J. A. Chatard, M. D.,	334
The Rise of the Present Conceptions as to the Cause of the Heart-Beat. By E. G. Martin,	338
The Partial Occlusion of Blood-Vessels, Especially of the Abdominal Aorta. A Preliminary Report by Dr. Halsted,	346
Notes on New Books,	347

THE EARLY DIAGNOSIS AND RADICAL CURE OF CARCINOMA OF THE PROSTATE.

BEING A STUDY OF 40 CASES AND PRESENTATION OF A RADICAL OPERATION WHICH WAS CARRIED OUT IN FOUR CASES.

By Hugh H. Young, M. D.,

Associate Professor of Genito-Urinary Surgery, The Johns Hopkins University.

The recent publication of Courvoisier, Wolff, Socin and Burckhardt, and Albarran and Hallé, have furnished a considerable stimulus to the study of cancer of the prostate, but although the disease has been shown to be much more frequent than was formerly supposed, and the pathological aspects have been well elucidated, practically nothing has been suggested in recent years as a routine operation for its radical cure.

Albarran's startling announcement that in 100 specimens of supposed benign hypertrophy he found more or less pronounced invasion of carcinoma in 14, seems not to have suggested the necessity of a radical excision, and even at this late date we find Pousson and Hawley advocating a mere enucleating prostatectomy, leaving behind the prostatic capsule, urethra, anterior commissure, the adjacent vesical mucosa and the seminal vesicles—structures which are manifestly in intimate contact with cancerous lobes.

The need of early diagnosis and radical methods of removal has been brought forcibly to the writer's attention in the past two years by the sad results arising from his failure to recognize, and to operate radically in six cases of early carcinoma of the prostate—several of which ought certainly to have been cured by the operation which he has since carried out in four cases. The object of this paper is to give in detail:

I. The six cases of early carcinoma in which the malignant nature of the disease was not recognized and a partial operation performed.

II. A radical operation, proposed as a routine for cases of cancer of the prostate, with histories of four operated cases.

III. A clinical and pathological study of 40 cases of carcinoma of the prostate.

IV. A comparison with cases in the literature in which operations for carcinoma of the prostate were performed.

V. Conclusions as to the practicability of early diagnosis and the radical cure of the disease.

I. Cases of Unrecognized Early Carcinoma with Partial Operation.

Case I. Male, aged 67. Admitted May 9, 1901. Duration of symptoms 2 years and 4 months. Uses a catheter, has had no hematuria and very little pain. Prostate much enlarged in left lateral lobe which is soft. Right lateral lobe not enlarged but indurated. Cystoscope shows enlargement of left lateral lobe and a small median bar. Diagnosis: benign prostatic hypertrophy. Bottini operation. Excellent result;

maintained for 2½ years. Returned three years after operation complaining of pain in bladder and urethra, frequent urination. Prostate much enlarged and indurated in both lateral lobes; seminal vesicles also involved. Cystoscope showed large irregular villous outgrowth in region of left lateral lobe which involved also the bladder. Death three months later. Autopsy showed the bladder invaded almost everywhere by malignant neoplasm, involving also the prostate. Microscope shows carcinoma.

Case II. E. G. W., aged 67. Admitted November, 1901. Difficulty of urination 2½ years duration. Catheterism for one year. Severe pain in bladder of late. Prostate considerably enlarged, smooth but very hard. Seminal vesicles not indurated. Residual urine 70 cc. Cystoscope shows large irregular calculus. Slight enlargement of lateral and median portions of prostate. Operation. Suprapubic lithotomy and complete prostatectomy. Recovery. Cure, maintained for 3 years and 10 months. Six months ago began to have pain in region of left kidney. Can now hold his urine for 5 hours, voids easily, no residual urine, bladder large, no pain in that region. Examination shows a large irregular mass beneath the left kidney. Liver enlarged and nodular. In region of prostate a very hard irregular mass. Cystoscope shows no intravesical obstruction or enlargement. Examination of specimen removed at first operation shows carcinoma of the prostate.

Case III. W. H., aged 56 years. Admitted May, 1902. Duration of symptoms two years. Now voids urine 30 times a day. No hematuria, no pain on urination, but severe pain is present in the region of the sacrum. Prostate enlarged and indurated in both lateral lobes. Left seminal vesicle also indurated. Cystoscope shows very little intravesical enlargement of prostate. Bottini operation. Five months later patient reported he had no difficulty in urination, but had pain in his spine and down his legs; this gradually grew worse and patient died six months later, evidently from carcinoma of prostate.

Case IV.—J. S., aged 68 years. Admitted August, 1902. Frequency and difficulty of urination for two years. Very little pain—no hematuria. Prostate much enlarged, large indurated nodule at upper end of each lobe. Residual urine 450 cc. Bottini operation, with good results for 20 months. Then return of difficulty; had to use a catheter. December, 1904; cannot void naturally, uses a catheter, has no pain. General glandular enlargement present. Prostate and seminal vesicles involved in a large irregular indurated mass. Cystoscope shows intravesical tumor.

Case V.—A. F., aged 60 years. Admitted September, 1902. Frequency of urination for three years. No pain, no hematuria. Prostate enlarged and indurated in both lobes. Left seminal vesicle also indurated. Cystoscope shows a slight hypertrophy of median and lateral lobes. Bottini operation. Excellent result maintained until January, 1904. After that difficulty and frequency of urination, pain and hematuria. Examination April, 1904. Prostate very large hard, nodular. Seminal vesicles involved on both sides. Cystoscope shows considerable outgrowth into the bladder. Patient died 8 months later.

Case VI.—J. J. S., aged 75. Admitted September 18, 1903. Frequency and difficulty of urination for three years. Pain in bladder, perineum and urethra—no hematuria. Uses catheter 6 times a day. Prostate considerably enlarged, very hard, slightly irregular, not tender. Seminal vesicles not palpable. Cystoscopic examination shows slight intravesical enlargement of prostate. Perineal prostatectomy, enucleation difficult owing to induration and adhesions. Immediate result good, and maintained for 9 months. Examination 10 months after operation. Difficulty of urination has returned. Residual urine 500 cc. Large irregular indurated mass involving prostate and seminal vesicle. Cystoscope showed marked increase in intravesical enlargement. Bottini operation. Improved. Death two months later. Tissue removed at prostatectomy showed adenocarcinoma.

Remarks.—In none of the foregoing six cases were the classical symptoms of prostatic carcinoma, as usually given, present. Pain was present only in the case with calculus and none had hematuria. The clinical picture of nearly all of the cases was that of the so-called sclerotic prostatic hypertrophy. Induration was a common finding in all the cases and the cystoscope showed very little intravesical hypertrophy. The failure to recognize the malignant nature of the enlargement in these cases caused the writer to be more careful, and to be suspicious of marked induration associated with little intravesical hypertrophy.

II. Four Cases of Carcinoma of the Prostate Recognized Early and Operated upon Radically.

In March, 1904, patient aged 70, who had suffered from frequency and difficulty of urination for one year, which had been unimproved by a Bottini operation three months before, presented himself. The prostate was hard, slightly nodular, induration extending into the region of the left seminal vesicle. The cystoscope showed only a slight intravesical prostatic enlargement. Pain had been slight and hematuria absent, but diagnosis of carcinoma was made because of the induration, and absence of intravesical enlargement. The patient gave his consent to a radical operation and the entire prostate, with the urethra and capsule, a cuff of an adjacent portion of the bladder including most of the trigone and the seminal vesicles, was removed in one piece. The operation was performed as follows with the kind assistance of Dr. Halsted:

An inverted V cutaneous incision was made in the perineum as in the operation employed by me for simple hypertrophy of the prostate—each branch of the incision being about two inches long. By blunt dissection the end of the bulb and central tendon were exposed, and the latter divided, exposing in turn the recto-urethralis muscle, the division of which gave free access to the membranous urethra behind the triangular ligament. Urethrotomy upon a grooved staff, was followed by introduction of the prostatic tractor, which was opened out

after it reached the bladder. While traction was made upon this instrument the rectum was carefully separated from the prostatic capsule by blunt dissection until the entire posterior surface of the prostate was brought into view. Up to this point the operator proceeded exactly as in the usual prostatectomy operation with the exception that the tissues around the prostate were more hemorrhagic and the wall of the rectum more closely adherent to the capsule of the prostate than usual. Examination of the prostate then showed much greater induration than I have ever encountered in the benign prostate. The rectum and periprostatic tissues were free from invasion. Complete excision was therefore decided upon, and carried out as follows: The handle of the tractor was depressed, thus exposing the membranous urethra anterior to it at a point where it was easily divided transversely with a scalpel, leaving a small stump of the membranous urethra protruding from the surface of the triangular ligament. By further depressing the handle of the tractor the pubo-prostatic ligament was exposed, and being very tautly drawn, easily divided by scissors, thus completely severing the prostate from all important attachments (except posteriorly) as shown in Fig. 1. The lateral attachments, which are slight, were easily separated by the finger. During these manipulations a moderate amount of hemorrhage was encountered (coming from the prostatic veins, particularly those just behind the triangular ligament in front of the prostate) but it was easily controlled by clamping several bleeding points, and applying pressure with gauze by means of an anterior deep retractor (see Fig. 3).

The posterior surface of the seminal vesicles were then freed by blunt dissection, the now mobile prostate being well out of the wound, as shown in Fig. 2. In this exposure of the posterior surface of the vesicles I was careful not to break through the fascia of Denonvilliers which covers not only the posterior surface of the prostate but also of the seminal vesicles, and forms I believe an important barrier to the backward growth of the disease.

The next step was to expose the anterior surface of the bladder, which was easily done by depressing the tractor and making strong traction. By this procedure, the bladder was drawn down so close to the skin wound that it was easily incised at a point in the middle line about 1 cm. behind the prostatovesical juncture, as shown in Fig. 3.

By means of scissors the division was continued on each side until the trigone was exposed, Fig. 4. After swabbing away the blood and urine the ureters were easily found and the line of incision carried across the trigone with a scalpel so as to pass about 1 cm. in front of the ureteral orifices.

While still making traction upon the prostate, the base of the bladder was pushed upward with the handle of the scalpel, thus exposing the anterior surface of the seminal vesicles and the adjacent vasa deferentia, Fig. 5, all of which were carefully freed by blunt dissection with the finger as high up as possible, so as to remove with the vesicles much circumjacent fat and areolar tissues on account of the lymphatics which they contained. The vasa deferentia after being drawn well down were picked up on a small blunt hook and divided with scissors as high up as possible, care being taken to see that the ureters were not in danger. After division of the vasa, the seminal vesicles were found to come down more readily, the deep adhesions were finally divided and the mass shown in the photograph, Fig. 6, was removed. As seen here in the side view, a portion of the membranous urethra, the entire prostate with its capsule intact, the seminal vesicles, 4 cm. of the vasa deferentia, and a cuff of the bladder 1 cm. wide along the anterior and lateral surfaces and 2 cm. wide in the region of the trigone has been removed in one piece. Fig. 7 shows the posterior view of the tissues removed.

There now remained a large defect to be repaired. The vesicle opening was about 8 cm. in diameter and had sunk far back into the depths. The stump of the membranous urethra had been obliterated by the compression of the anterior retractor so that it was necessary to insert a soft rubber catheter through the urethra from the meatus to discover it. The anterior wall of the vesicle opening was then caught with forceps, and with no great traction I was surprised to find how easily it could be drawn down to the membranous urethra, where an anastomosis was readily made as shown in Fig. 8. The first suture was placed by inserting the needle into the triangular ligament above the urethra and out through the anterior wall of the membranous urethra, then through the anterior wall of the bladder in the median line, from within out, care being taken to include only the submucosa and muscle. When this suture was tied, the median line of the anterior wall of the bladder was drawn to meet the median line of the roof of the remaining membranous urethra, the knot outside, and the thread left long.

Lateral sutures, similarly placed (including the periurethral muscular structures below), and two posterior sutures completed the anastomosis of the membranous urethra with a small ring into which the anterior portion of the margin of the vesical wound had been fashioned by the tying of the sutures, as shown in Fig. 8. The remainder of the vesical wound now presented as a longitudinal opening which was easily closed by sutures, placed as shown in Fig. 8, thus completely closing the defect and replacing the prostatic urethra with a funnel-shaped process made from the bladder wall. The sutures used were silk, one end of each being left long and brought out of the wound so that they could be extracted later (since then I have found alternate sutures of catgut and silk-worm gut, also left long, the best). After light gauze packing had been placed in various portions of the wound, the levator ani muscles were drawn together with catgut (two sutures) in front of the rectum and the skin wound closed on each side with interrupted catgut sutures leaving only a small portion open at the angle in front for exit of the gauze drainage. The rubber catheter (which was of considerable service in making the anastomosis of the urethra and bladder) was fastened in place, by adhesive plaster around the penis, and the patient was returned to the ward. During the operation he received 1000 cc. salt solution

infusion beneath the breast, and his condition throughout was good, pulse varying from 65 to 92, and 80 at the end of the operation which required two hours.

A study of the specimen removed showed adenocarcinoma involving the entire prostate, the region between the seminal vesicles and the inferior surface of the excised trigone and the vasa deferentia. The capsule of the prostate and the bladder at upper limit of excision were free, but along the left vas deferens the disease extended to the upper limit of the incision 4 cm. above the prostate.

Convalescence.—Patient convalesced well. Left the hospital May 30, 1904. Perineal wound healed tight; no difficulty in urination; able to hold his urine for three or four hours at night; incontinence in the day.

December 22, 1904. Condition of patient excellent until 2 months ago when he began to suffer pain in the urethra. Examination shows three calculi in the bladder. Operation, litholapaxy. One calculus was found attached to a silk ligature and in removing this the mucous membrane of the bladder was torn. This was followed by perineal abscess, extravasation of urine and death four weeks later. Autopsy showed excellent union between bladder and urethra. No recurrence in bladder, but behind bladder along left vas deferens was a small area of carcinoma. No carcinomatous glands present.

Case VIII.—W. R., No. 16,675. Admitted September 14, 1904, aged 64. Frequency and difficulty of urination for three years. Has to use catheter now. No hematuria, no pain. Prostate moderately enlarged, smooth, very hard but not nodular. Between the two seminal vesicles an indurated plateau continuous with the prostate below. No indurated glands or lymphatics. Cystoscope showed slight intravesical enlargement of median portion. Diagnosis: carcinoma of the prostate. Operation September 23, 1904. Total excision of prostate, seminal vesicles, portion of the vasa deferentia, cuff of the bladder, the entire trigone including the ureteral orifices. The excision was carried above the ureteral orifices because the bladder wall there felt indurated and the operator thought it was involved. Examination of the tissue removed, however, showed that this was a mistake, and that only the anterior part of the trigone was invaded by the disease. Transplantation of the ureters was not necessary because the intramural portion had not been completely removed. Anastomosis of anterior wall of bladder and urethra was made as in case VII. The patient convalesced badly, early showed symptoms of pyelitis and died November 8, 1904.

Autopsy showed ascending infection of both kidneys and besides that chronic endocarditis, perihepatitis, splenitis, pancreatitis. Careful examination showed that the carcinoma had been entirely removed at operation. No metastatic glands present. The patient would almost certainly have been cured had the operator not excised the ureteral papillæ.

Case IX.—S. R. B., aged 65. Admitted February 4, 1905. Frequency and difficulty of urination for four years. Now voids every few minutes. Intermittent pain in left hip and thigh for two years. Dull pain in back, bladder, perineum, and rectum. Has never had hematuria. Examination: No glandular enlargements. Prostate considerably enlarged, smooth but very hard. Induration involving the lower end of the seminal vesicle on each side with a narrow plateau between them above the prostate. Cystoscope shows very slight enlargement of the median portion of the prostate. Diagnosis of carcinoma of the prostate made upon the induration involving also the seminal vesicles and the area between them, and the absence of intravesical prostatic enlargement.

February 16, 1905. Radical operation was carried out as in case VII. Patient made an excellent recovery. Was entirely relieved of pain. Perineal wound healed tight. Urine comes entirely through the urethra.

Examination June 24. Condition excellent. Voids urine about every 2 hours. Has no incontinence at night, but in the day urination is imperative when desire comes on. Examination shows no evidence of recurrence.

Study of the tissue removed at operation shows adenocarcinoma involving the prostate, both seminal vesicles, vasa deferentia and the tissues between them and the excised portions of the bladder.

Case X.—J. E. D., aged 64. Admitted May 12, 1905. Difficulty and frequency of urination for one year. For two months has had to use a catheter. No pain in region of bladder, rectum, back or legs. Has not lost weight. No hematuria. Healthy looking man. No glandular enlargement. Prostate considerably enlarged, particularly left lateral lobe which is very hard and tender. The seminal vesicle is indurated on this side. Residual urine about 400 cc. Cystoscope shows small enlargement of the median portion of the prostate. Diagnosis of carcinoma made on induration, extending into the region of the seminal vesicle and the absence of marked intravesical enlargement.

May 16, 1905. Radical operation carried out as in Case VII. The patient made an excellent convalescence. Perineal wound healed in 5 weeks. Discharged from hospital in six weeks. General condition excellent. Suffers no pain, urine passes entirely through the urethra. Rectal examination negative. Patient feels well, but as yet has no control over urine.

Examination of tissues removed at operation showed adenocarcinoma of prostate, of a portion of the seminal vesicle, and of lower portions of vasa deferentia. One excised gland was also carcinomatous. The trigone, the capsule of the prostate and perivesicular fat were free from disease.

III. A Clinical and Pathological Study of 40 Cases of Cancer of Prostate.

Nineteen of these are taken from the records of the Johns Hopkins Hospital, service of Dr. Halsted, whom I wish to thank for the privilege of reporting them. Twenty-one are from the records of my private cases.

Age.—The ages were as follows:

1				53 years.
8	between	55	and	59.
12	"	60	"	64.
11	"	65	"	69.
6	"	70	"	74.
1				75 years.
1				76 "

As seen here 57% are between 60 and 70 years of age and 95% between 55 and 75.

Onset.—In 28 cases the first symptom was frequency of urination; in 11 associated with more or less difficulty in voiding. Pain was noted at onset in only 12 cases and in four of these was only a slight burning in the bladder. Hematuria ocurred only three times at onset.

Later symptoms.—Pain was present in 27 cases, not present in 8, not noted in 5. It occurred 11 times in the bladder, 7 times in the penis, 4 times in the perineum and the rectum, three times each in the leg, thigh, sacrum, testicle, and abdomen, twice in the hip and groin and once each in the knee and sole of the foot. Cases in which a seminal vesicle was involved showed pain radiating at times down the sciatic nerve.

Hematuria.—This is stated to have been present in only 8 cases and in 4 of these the bladder was involved.

Retention of urine.—In all cases but one some residual urine was present. In 20 cases incomplete retention, varying from 50 to 850 cc. In 7 cases complete retention requiring catheter life and in 6 cases intermittent complete retention. In 8 cases no note was made on this point.

The prostate.—This was considerably enlarged in 24 cases, moderately enlarged in 9, slightly enlarged in 5, hard in 30, in places hard and in others soft in 5, and everywhere soft in 3 cases. It was nodular in 17 cases, smooth in most of the others. Marked tenderness was noticed only once in the 40 cases. In those cases which were not far advanced in the disease the prostate usually presented a smooth rounded surface, but was markedly indurated. This induration was often of stony hardness and the contrast with that of benign hypertrophy was very marked.

Seminal Vesicles.—It was in the region immediately above the prostate on each side in which the most significant changes were found, induration of one or both of the seminal vesicles being present in 29 cases. In recent cases, where more careful notes have been made, a plateau of induration in the intervesicular space has been noted in 10 cases. This induration is positive evidence of the spread of the disease between the vasa deferentia and the bladder after breaking through the capsule of the prostate at the base. Specimens show, however, that it is often well limited.

Rectum.—This was involved by the growth in but two cases and in only one of these was the mucous membrane ulcerated.

Bladder.—Careful cystoscopic examinations were made in 23 cases and in 7 the bladder wall was involved generally in the region of the trigone adjacent to one or both of the ureteral orifices, five times in the form of intravesical tumors, and twice of superficial ulceration. Examination of the bladder by suprapubic cystotomy showed a nodular elevation of the trigone in one case, the other case being normal. Two autopsies showed the bladder to be uninvolved. There was no intravesical enlargement of the prostate shown with the cystoscope in 5 cases. In 12 cases a very slight elevation of the median portion was present. In 3 cases a small median lobe, and in only one case a fairly large median lobe. The lateral lobes were at all intravesically enlarged in only four cases. In six cases the intravesical prostatic outgrowth was villous in type and associated with tumor of the bladder in 3 cases.

Glandular involvement.—Enlarged glands have been noted in only 11 of the 40 cases as follows: Deep pelvic glands four times, inguinal five times, iliac twice, sacral twice, axillary once, epitrochlear once. This corresponds to the findings of Kaufmann who discovered involvement of the pelvic glands in only 27 out of 100 autopsies. In one of our cases in which the tibiæ, vertebræ, and ribs contained numerous metastases, only one metastatic gland, and that a bronchial gland, was found.

Loss of weight was considerable in 18 cases.

Considerable increase in thickness of the suburethral portion of the prostate and also of the tissues between the trigone and the rectum has been shown in many of these cases by examination with the finger in the rectum and cystoscope in the urethra, the beak turned backward. In a number of cases the intervesicular mass and induration have prevented one from feeling the beak of the instrument in the bladder.

The pathology.—That carcinoma may begin in a benign adenomatous hypertrophy is shown in Case I. Generally induration is present in both lobes when the patient is first seen, but the disease remains localized within the prostatic capsule for months and often for several years. The capsule of the prostate is very thick and strong, especially in its posterior portion, where it is rendered much thicker and stronger by the incorporation of the aponeurosis of Denonvilliers, which covers intimately the posterior surface of the prostate and seminal vesicles. At the base of the prostate there is a space, between the seminal vesicles and the bladder, where the prostatic capsule is weakest and it is here in nearly all of the cases that the disease spreads first beyond the confines of the prostate. At the same time it usually travels up the lumina of the vasa deferentia and seminal vesicles forming a plateau of induration above the ordinary confines of the prostate, generally marked by a concave superior border and a notch on each side where it joins the lateral lobes. The posterior surface of the anterior part of the trigone becomes invaded from this mass, and it may finally penetrate the entire wall of the bladder and show itself intravesically generally as a small tumor or ulceration in the region of one or both ureteral orifices. The disease spreads laterally along the nerve sheaths and the lymphatics, indurated cords of which are often found leading upward and outward above the prostate along the lateral wall of the pelvis. The pelvic glands are, however, not often found involved.

Only occasionally does the disease present into the bladder

in the shape of considerable intravesical enlargements around the prostatic orifice.

IV. A Comparison with the Cases in the Literature in which Operations for Carcinoma were Performed.

I find 26 cases of primary carcinoma of the prostate reported, and to these six cases are here added, excluding those in which the Bottini operation was performed. Cases of carcinoma of the rectum involving the prostate and sarcoma of the prostate, which have been included by Oraison, Pousson, and Hawley, have no place here, but I have referred to them briefly to show why they should be excluded. I have grouped the cases according to the operation performed as follows:

Partial operations, (enucleation, partial excision or curettage), by perineal route, 12 cases, by the suprapubic route 9 cases.

Radical operations.—A. Complete excision of the prostate, the entire bladder and the seminal vesicles with transplantation of the ureters into the rectum, one case, by Küster, with death in 5 days.

B. Complete excision of the prostate, probably the seminal vesicles, most of the bladder with transplantation of the ureters into the remaining vertex of the bladder, one case, Harris. Recurrence and death two months later of pneumonia.

C. Complete excision of prostate, seminal vesicles, adjacent portion of the bladder leaving the ureters intact and anastomosing bladder opening to membranous urethra, four cases, Young (reported above).

D. Excision of prostate without seminal vesicles, three cases. Immediate death, one case. Recurrence and death in the other two cases.

E. Rectum and prostate involved by carcinoma, 5 cases. Immediate death, 3 cases. Two cases of primary carcinoma of the rectum involving only slightly the prostate, said to be cured after operation.

F. Sarcoma of the prostate, three cases. Immediate death, one case. Recurrence and death 9 months and four years, two cases.

Remarks.—A study of these cases shows conclusively that partial operations are of no permanent utility in cancer of the prostate. Among the 12 cases in which partial operation was done through the perineum, 9 died of recurrence and the other three cases were followed only one, three and nine months respectively. Of the 9 operated upon by the suprapubic route 6 had recurrence, one was not followed and two were said to have been fully cured one year after the operation, although only a median lobe was removed in each case. In the three cases in which the prostate was completely excised, but the seminal vesicles and the adjacent portion of the trigone were not removed, death resulted in all three cases, once from operation, twice from recurrence.

Küster's case associated with multiple vesical tumors cannot rightly be included in the results of operations upon the cancerous prostate. His operation of complete excision of the bladder and prostate, with transplantation of the ureters into the rectum ended in death in 5 days. When the disease has spread beyond a localized invasion of the bladder adjacent to the prostate, a radical operation is out of the question, and such procedures as that of Küster are useless if not always certainly fatal. Those in which the rectum is invaded in the prostatic tumor are in the same category—useless and harmful. Of the five cases reported only one was cured and in this case the carcinoma started in the rectum and involved the prostate only superficially. Harris' case is very interesting, but simply shows the truth of the above statements. The remaining class—those in which the seminal vesicles and cuff of the bladder were excised in one piece with the prostate, comprises only the four cases of the writer. There has been no operative mortality. One case (VIII) died six weeks after the operation as a result of an operative mistake—excision of the lower half of the intramural course of the ureters along with the trigone because it felt like it was invaded. Careful study of the specimen removed, however, showed that this was a mistake; that the trigone was only invaded near the prostatic orifice, and that the excision had been much more extensive than was necessary. This was fully confirmed at autopsy as careful search failed to reveal any carcinoma, regional or glandular, and sections of structures adjacent to the prostate were negative microscopically. This case would probably have been cured by the operation had the valvular ends of the ureters not been removed.

Case VII died one year later as a result of litholapaxy. The operative specimen in this case showed cancer up to the upper limit of excision (above the left seminal vesicle) and the autopsy showed a very small area of carcinoma behind the bladder above this point. No invaded glands and no other evidence of cancer was to be found. The case had been subjected to a Bottini operation, in another city, three months before. A radical operation at that time would probably have cured him.

The other two cases (IX, X) have been operated upon 6 and 2 months respectively—too recent for consideration; however, both are comfortable and free from recurrence so far. It has been surprising to see how easily this deep and extensive operation can be carried out and particularly how little post-operative shock and discomfort is caused.

Early diagnosis.—The question of cure depends upon early diagnosis. As shown above, this is often difficult because of the absence of characteristic symptoms and signs. When severe pain and hematuria are associated with a very hard prostate with upward prolongation of the induration into the region of the seminal vesicles on each side the nature of the disease is evident at once. When, however, the symptoms are those of ordinary hypertrophy and the seminal vesicles and the vesicular region are normal in feel the diagnosis is often difficult. After a careful review of these cases I now feel that a markedly indurated prostate producing obstruction in a man over 50 years of age should be viewed with suspicion. If it is of stony hardness it is very apt to be cancerous, especially if the cystoscope shows little or no enlargement intravesically as in the ordinary hypertrophy. In

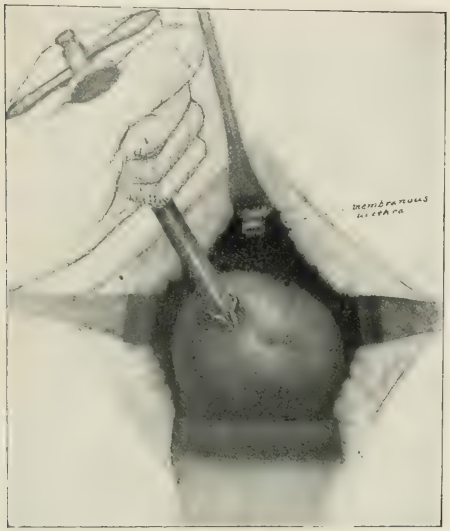


FIG. 1.

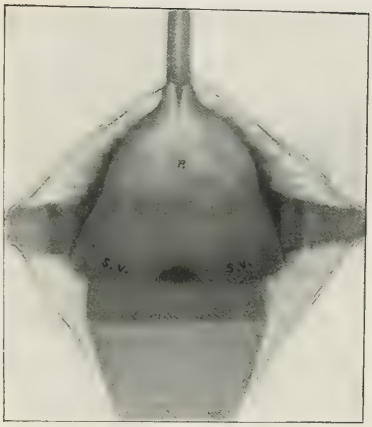


FIG. 2.

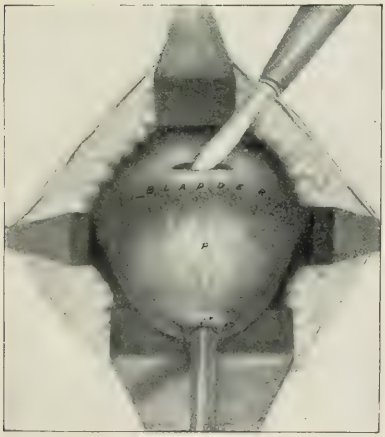


FIG. 3.

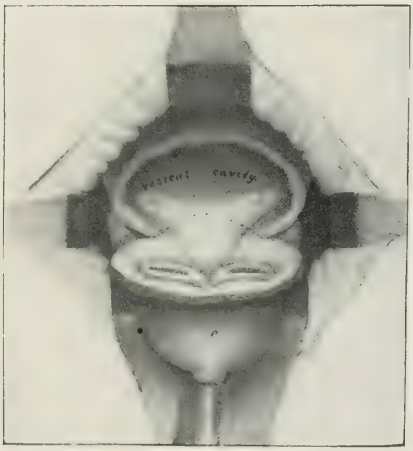


FIG. 4.



Fig. 5.

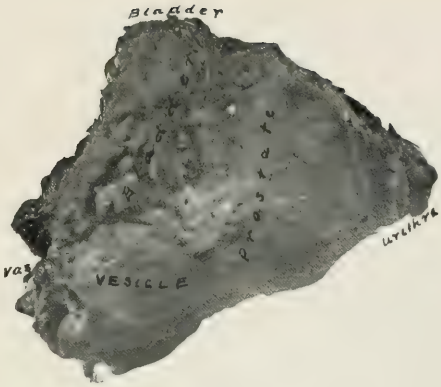


Fig. 6.



Fig. 7.

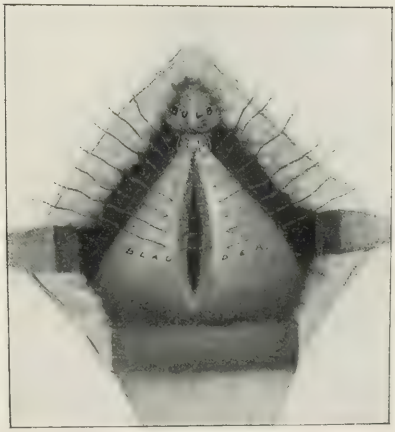


Fig. 8.

such cases I proceed to expose the posterior surface of the prostate as in the ordinary prostatectomy operations, palpate the prostate directly and if I find the posterior capsule more adherent to the rectum, the tissues more hemorrhagic and the consistency of the prostate much more indurated than in simple hypertrophy, I am able generally to make the diagnosis of carcinoma without cutting into it, and proceed at once with the radical operation.

In a recent case after exposing the prostate I was still uncertain as to malignancy and therefore made a longitudinal incision into the prostate on each side of the urethra as if for the usual prostatic enucleation, and then excised a slice of the lateral lobe parallel to the cut. Macroscopic examination of this showed the characteristic appearance of prostatic carcinoma—glandular yellowish dots and lines in a paler, more fibrous stroma, and a frozen section, made at once and stained, showed definite adenocarcinoma invading the intra-glandular stroma. It only required 6 minutes to make and stain the frozen section, and I therefore propose the method as one of practical utility in all cases where the operator is in doubt as to the character of the enlargement. When the presence of cancer is demonstrated the capsular incisions are to be closed at once and the radical operation carried out.

In view of the six cases detailed at the beginning of this paper in which a mistaken diagnosis was made I propose in all cases in the future to study the cut surface of the prostatic lobes immediately after their enucleation at the operating table, and if there is the slightest suspicion of malignancy to have frozen sections made at once. In very few cases will the wait of 5 minutes or more make any difference to the patient. In cases where the prostate is indurated, if only in part, this operating-room-study of the fresh tissues is of the greatest importance. I feel sure that several of my first six cases might have been saved by the radical excision which would now follow such a course.

Conclusions.

The following conclusions may be drawn from this study of 40 cases. Carcinoma of the prostate is more frequent than is usually supposed—occurring in about 10% of the cases of prostatic enlargement, as shown also by Albarran. It may begin as an isolated nodule in an otherwise benign hypertrophy or a prostatic enlargement which has for many years furnished the symptoms, and signs of benign hypertrophy may suddenly become evidently malignant.

Marked induration, if only an intralobar nodule in one or both lobes of the prostate in men past 50 years of age should be viewed with suspicion, especially if the cystoscope shows little intravesicular prostatic outgrowth, and pain and tenderness are present.

The posterior surface of the prostate should be exposed as for an ordinary prostatectomy, and if the operator is unable to make a positive diagnosis of malignancy, longitudinal incisions should be made on each side of the urethra (as in prostatectomy) and a piece of tissue excised for frozen sections, which can be prepared in about six minutes and examined by the operator at once. If the disease is malignant the incisions may be cauterized and closed and the radical operation performed.

Cancer of the prostate remains for a long time within the confines of the lobes, the urethra, bladder and especially the posterior capsule of the prostate resting inviolate for a considerable period. Extraprostatic invasion nearly always occurs first along the ejaculatory ducts into the space immediately above the prostate between the seminal vesicles and the bladder and beneath the fascia of Denonvilliers. Thence the disease gradually invades the inferior surface of the trigone and the lymphatics leading toward the lateral walls of the pelvis, but involvement of the pelvic glands occurs late and often the disease metastasises into the osseous system without first invading the glands.

Cure can be expected only by radical measures and the routine removal of the seminal vesicles, vasa deferentia and most of the vesical trigone with the entire prostate as carried out in four cases by the writer and fully described by the illustrations is shown to be necessary by the 40 cases, including 8 autopsies and 10 operations, reported above.

The four cases in which the radical operation was done demonstrated its simplicity, effectiveness and the remarkably satisfactory functional results furnished.

ACTION OF THE TOXIC AGENT OF LOBAR PNEUMONIA: THERAPEUTICS.[1]

By Walter V. Brem, Jr., M. D.,

Medical House Officer, The Johns Hopkins Hospital.

Introduction.

The data that have been accumulated during this study are incomplete and, consequently, the inductions made therefrom are often inconclusive. Nevertheless, since many definite questions for further investigation have arisen, it has seemed worth while to present the facts, together with their possible interpretations and therapeutic indications.

In discussing the changes in functional activity occurring in pneumonia, it has been found convenient to divide the cases here presented into two groups, according to the gravity of the symptoms. To the first group belong the mild cases;

[1] Read before the Johns Hopkins Medical Society, June 5, 1905.

to the second, the severe and fatal cases. For convenience, also, the causative factor, which in this disease brings about the changes in question, will be designated as the toxic agent. The dots in the curves of the charts here studied represent, for the most part, averages of daily two-hour observations. But dots in blood-pressure curves and in every place where the hour is stated represent only single observations. The blood-pressure instrument used was the Riva-Rocci with 12 cm. cuff. Normal systolic and diastolic blood-pressures are those determined by Brush (1). Systolic pressure was obtained by the method of obliteration; diastolic, by Strassburger's method (2). All cases studied, except one (Chart V), were under my immediate care in the wards of the Johns Hopkins Hospital.

hours preceding improvement, at which time all the other curves fall synchronously. Besides these phenomena, there are nervous manifestations at onset or during the acute illness, namely, headache, chill, restlessness, wakefulness, convulsions frequently in children, and occasionally active delirium; all manifestations of excitation of the central nervous system.

Respiration.—Acceleration of the respiratory-rate may be due to one or more of several causes, chief of which are pain, fever, and toxæmia (Osler). Pain in the side, exaggerated by breathing, causes voluntary restriction of the respiratory movements and there is compensatory hastening. But cases having no pain (Charts II, VII), and others in which pain has been relieved by the ice bag and analgesics, show similar acceleration. Fever, also, aids in producing the condition; but not infrequently it happens that the respiratory-rate increases while temperature falls or remains unchanged, or the change in one is not in proportion to the change in the other (Charts III, IV, X). Moreover, in typhoid fever, when temperature reaches a high degree, there is no similarly marked acceleration of the respiratory-rate, which often remains normal throughout the course of the disease. It is easier to

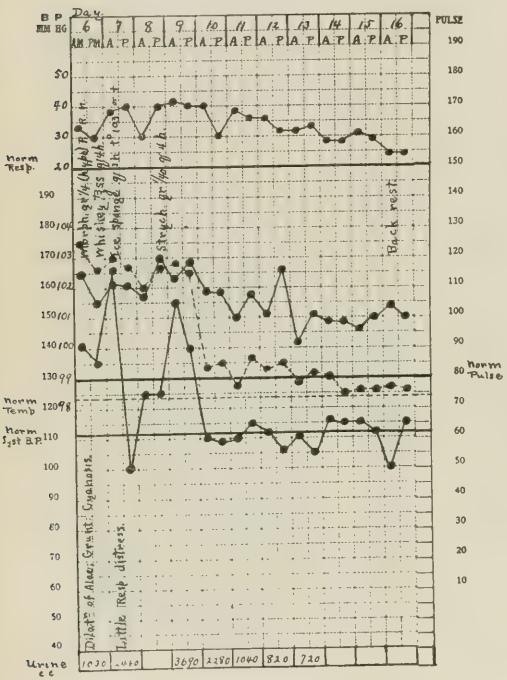


Chart I.—Merriweather, male, colored, age 56, recovery.

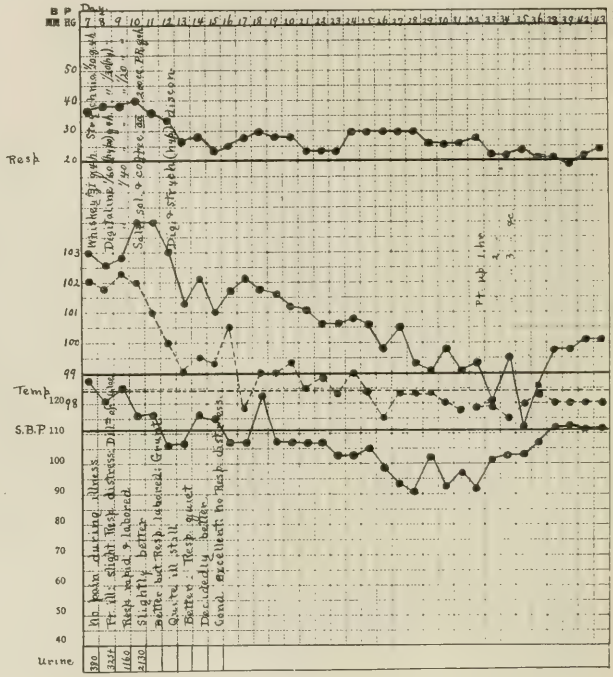


Chart II.—Jenkins, male, colored, age 28, recovery.

Mild Action of the Toxic Agent.

The mild cases are represented by Charts I, II, V, VII, which show a series of familiar phenomena. Here, the temperature is elevated; the respiratory-rate and pulse-rate are accelerated; and both systolic and diastolic (Chart VII) blood-pressures are high. The urinary output is diminished at first, but there is a great increase during the twenty-four

think, therefore, that the respiratory-rate is not greatly dependent upon either pain or temperature, but that the acceleration is in response chiefly to the action of the toxic agent upon the respiratory center.

In addition to acceleration of the rate, one finds by examination of the patient that the accessory respiratory muscles are brought into action, there is an expiratory grunt and dilatation of the alæ nasi with inspiration, and the vesicular murmurs in uninvolved portions of the lungs are intensified. It appears, then, that there is an increase not only in the rate

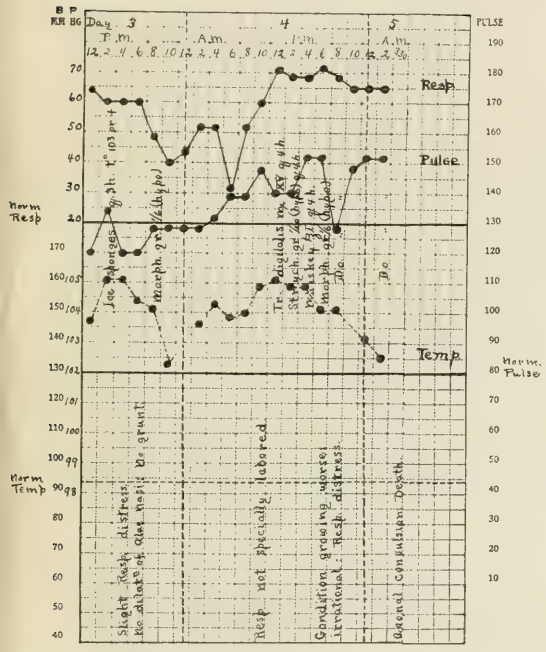


Chart III.—Bunch, male, colored, age 23, death.

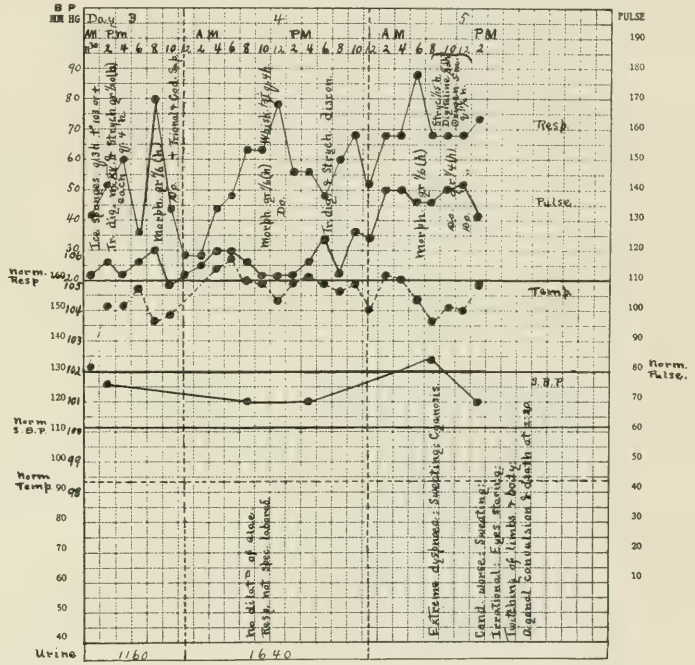


Chart IV.—Harris, male, colored, age 38, alcoholic, death.

but in the intensity, also, of the respiratory movements; that is, there is hastened and intensified activity of the respiratory center. Therefore, the action of the toxic agent upon the center may be regarded as that of a stimulant.[2]

Circulation.—The circulatory phenomena are acceleration of pulse-rate and high systolic blood-pressure. Diastolic blood-pressure, likewise, in the one case in which observations were made, was high, but this cannot be used as a demonstration that it is usually elevated. Evidence of high pressure in the pulmonary vessels, also, may be found in the almost constant accentuation of the pulmonic second sound.

Acceleration of pulse-rate may result partially from pain, restlessness, and fever. The rate remains rapid, however, when pain and restlessness are absent (Charts II, VII) or relieved (Charts I, III, IV, IX, X). These charts show further that, like the respiratory-rate, the pulse-rate does not vary constantly with temperature, but that very wide differences frequently occur. Therefore, it is probable that this disturbance, also, is due chiefly to the action of the toxic agent upon the circulatory mechanism. It may result from depression of the cardio-inhibitory center or from increased irritability of the heart muscle, of the cardio-accelerator center, or of both.

Depression of the cardio-inhibitory center would offer a sharp contrast to the general nervous excitation and apparent stimulation of the respiratory center, while in perfect harmony with other phenomena is the supposition that the action of the cardio-inhibitory center, even if its irritability be increased, is overborne by the more intense action of the toxic agent upon the heart muscle and accelerator center. Some

[2] "Drugs which increase the activity of any organ or function are said to *stimulate* it. Stimulation is properly used to indicate an increase in the specialized function of a cell. . . . Irritation, on the other hand, is used rather in reference to the changes in the conditions common to all forms of living matter, that is, it indicates a change in the growth and nutrition of the cell, rather than in the specialized functions" (Cushny). The terms will be used in these senses throughout the present paper.

confirmation, possibly, of this view may be found in the fact that digitalis, exhibited during the stage of excitation, does not slow the pulse-rate. This seems to indicate that there are forces present which counteract the primary stimulating action of the drug upon the cardio-inhibitory center.

Besides rapidity of heart-rate, examination of the patient reveals a strong cardiac impulse and loud heart sounds with marked accentuation of the pulmonic second. The group of phenomena strongly suggest intensified cardiac activity and increased work. This is rendered the more probable by the fact that systolic blood-pressure is high; for an increase of systolic pressure indicates an increase of cardiac work, unless there is a greater rise of diastolic pressure. That the rise of diastolic pressure during this stage of pneumonia is not as great as that of systolic pressure is indicated by the large, bounding pulse. Such a pulse, with systolic pressure high, means a large cardiac output and an increased product of the formula for cardiac work (mean blood-pressure by cardiac output).

Summary.—The mild action of the toxic agent possesses, then, all the features of a stimulation of the central nervous system and heart muscle, evidence of which is found in cerebral excitation and in increased activity of the respiratory and circulatory mechanisms.

Intense Action of the Toxic Agent.

In the severe and fatal cases (Charts III, IV, IX, X) the phenomena vary in different individuals according to the relative susceptibility of different organs. Often there is evidence of cerebral depression, which results, if the theory of stimulation be correct, from overstimulation and enfeeblement. The patient looks toxic, there are stupor, low delirium, later coma, and occasionally involuntary passage of urine and fæces. In other cases the mind may remain active until the end. Temperature may rise before death (Chart IV, day 5, 2 p. m.), or suffer a decided fall (Chart III, days 4 and 5); again it may remain practically unaffected while the respiratory or circulatory condition is grave (Charts IX, days 4, 5, 6, 7; X, days 8, 9). These variations, also, may depend upon the degree of excitation and overstimulation of the heat-regulatory centers.

Respiration.—It is probable that in the majority of cases the respiratory function is that most gravely affected. The rate usually ranges between 40 and 80 per minute; the accessory muscles of respiration are brought more violently into action; the vesicular murmurs become more intense; the movements become progressively shallow; breathing necessitates great effort and becomes labored; and cyanosis appears, evidence of deficiency of O and accumulation of CO_2 in the blood, a condition which may be termed respiratory insufficiency.

It is an interesting and important point that respiratory insufficiency may become established even under strong stimulation when the total quantity of air respired is much increased. The factors concerned in this are two: (1) The depth of the respiratory movements tends to vary inversely with the rate, and (2) the capacity of the bronchial tree, about 140 cc., remains a constant figure, while the tidal wave of respiration decreases in volume; that is, the quantity of fresh air actually entering the alveoli with inspiration is the portion of respired air that suffers diminution when the volume of the tidal wave is decreased.[a] Bearing these facts in mind, a glance at the table below will show that, with progressively rapid and shallow movements, the alveolar portion of respired air diminishes with far greater rapidity than the total volume of the tidal wave.

TABLE I.

Condition	Tidal wave	Rate per min.	Total per min.	Capacity of Bron. tree	Alveolar portion of tidal wave	Rate per min.	Total per min.	%	Equivalent volume % of atmospheric O
1. Normal	500 × 20 = 10,000cc.			140cc.	360 × 20 = 7200cc.			100	21.0
2. Depth in exact inverse proportion to rate	250 × 40 = 10,000cc.			140cc.	110 × 40 = 4400cc.			61+	12.8
3. Stimulation	200 × 60 = 12,000cc.			140cc.	60 × 60 = 3600cc.			50	10.5
4. Strong stimulation	190 × 80 = 15,200cc.			140cc.	50 × 80 = 4000cc.			55.5	11.6+

Now, 13 volume per cent of atmospheric O is necessary to raise alveolar O-tension to the point where normal O-absorption by blood occurs. In conditions 3 and 4, the alveolar O-tension is reduced to 50 and 55.5 per cent, respectively, of normal; that is, to points equal to alveolar O-tension that would be produced by atmospheres containing only 10.5 and 11.6 + volume per cent of O. Therefore, in conditions 3 and 4, there is respiratory insufficiency, although the total volume of air respired is increased considerably in the former condition and greatly in the latter. The table deals only with mechanical mixture of the gases, which is of far greatest importance in the interchange between the atmospheric and alveoli (4). As to the less important factor of diffusion, it can be shown by another calculation that, if the inspired air enters the alveoli gradually and with but slight mechanical mixture, diffuse conditions are correspondingly less efficient with rapid and shallow respiratory movements.[a] Owing to the same causes there is diminished elimination of CO_2 with corresponding increase of alveolar CO_2-tension, and consequent accumulation of this gas in the blood. There is added, thus, to the action of the toxic agent an intensification of the

[a] It is true that a volume of air equivalent to the tidal wave, normally about 500 cc., does enter the alveoli with each inspiration. But the first portion entering is the 140 cc. of vitiated alveolar air that filled the bronchial tree at the end of the preceding expiration. Therefore, in a normal inspiration, only 360 cc. of atmospheric air enters the alveolar. So, in any given inspiration, the alveolar portion of respired atmospheric air may be obtained by subtracting 140 cc. from the volume of the tidal wave.

[a] Rapidity of diffusion varies with the area and with the time of contact. Since a smaller quantity of air enters the alveoli with rapid and shallow breathing, the time of its passage in and out is correspondingly less. The area of contact cannot be estimated, but it is probable that it, also, is reduced somewhat.

natural physiological stimulus to the respiratory center. This tends further to increase its work and to lessen the efficiency of respiration. A vicious circle is thereby produced and enfeeblement of the center follows, passing on rapidly towards asphyxiation or exhaustion.

Circulation.—The circulatory condition may, and often does, remain excellent throughout, and, as a rule, the circulatory mechanism is much less affected than the respiratory. The pulse-rate, under more intense action of the toxic agent, becomes more markedly accelerated (Charts III, days 4, 5; IV, days 4, 5; IX, days 6, 7; X, days 7, 8, 9). But even with great acceleration, systolic blood-pressure may remain above normal until the end (Chart IV, days 3, 4, 5), indicating that the heart's action has not become enfeebled.

In other cases, the circulatory mechanism may bear the brunt of the attack or be affected simultaneously with the respiratory mechanism. In addition to the rapid pulse-rate, systolic blood-pressure falls even if there be associated respiratory insufficiency with asphyxial stimulation of the vaso-constrictor center (Chart IX, days 4, 5, 6); the extremities become cyanosed; the pulse becomes "thready," indicating lessening of pulse-pressure with which the urinary output tends to vary (3); the heart's action becomes enfeebled and the sounds soft, the pulmonic second loses its accentuation, and the right ventricle may become dilated. These phenomena are to be accounted for, apparently, by overstimulation and overwork leading to enfeeblement and insufficiency of the circulatory mechanism. The probable results are lessened metabolism and lessened power of resistance; decreased urinary output with decreased elimination of the toxic agent; and sometimes the onset of œdema of the lungs, which may be the terminal event. In other cases, enfeeblement of the mechanism may pass on quickly to exhaustion and death.

Systolic blood-pressure, it has been said, falls with the establishment of circulatory insufficiency, even if there be an associated condition of respiratory insufficiency (Chart IX, days 4, 5, 6). If, however, the circulatory condition remains good when respiratory insufficiency becomes established, systolic blood-pressure rises, owing to asphyxial stimulation of the vaso-constrictor center (Charts IV, day 5; IX, day 7; X, day 9). The change in blood-pressure of Chart IX, day 7, was due to the administration of digitalis every four hours. It appears that the drug improved the condition of the heart so that blood-pressure became elevated, as is normally the case with asphyxial stimulation. It is evident, therefore, that systolic pressure may be either high or low when the situation is critical, and that in itself it is of little value as an indicator of the patient's condition. Considered with the respiratory phenomena, however, it is of great value in determining the circulatory condition and the treatment to be pursued.

Summary.—The phenomena of the mild action of the toxic agent pass over into phenomena of the more intense action. These appear to be expressions of intensified stimulation, which aggravates the condition of increased functional activity and tends to induce overwork, enfeeblement and exhaustion. The mechanisms concerned break down prematurely because they have been subject, also, to the irritative destructive action of the toxic agent.

The main causes of death are (1) respiratory insufficiency terminating in asphyxiation or in exhaustion of the respiratory center, and (2) circulatory insufficiency, which leads, presumably, to accumulation of the toxic agent, and which may induce œdema of the lungs or end in exhaustion of the heart muscle.

Therapeutics.

Having studied in typical cases the changes in functional activity brought about by the action of the toxic agent, one is now in a position to discuss measures to be used in combating its influence. The ideal therapy, of course, would be to prevent destruction of tissues by neutralizing or destroying the toxic agent, but with the possibility of this the present study is not concerned. In lieu of it, efforts must be directed towards eliminating the agent or ameliorating its harmful influences.

Elimination.—Undoubtedly the most efficient means of eliminating the toxic agent is by *internal hydrotherapy.* The effort is made to pass through the circulation the largest quantity of fluid possible in the hope that as it is passed through the kidneys the toxic agent will be carried, in one way or another, along with it. If there is a soluble toxin, this is a reasonable hope; for during the acute illness, almost constantly the albumin molecule, a normal constituent of blood, passes through the kidneys. Since an effort is made to eliminate abnormal substances in blood, it is reasonable to suppose that the abnormal toxin molecule would be more readily eliminated than the normal albumin molecule. If there is no soluble toxin, *B. typhosus* sometimes, at least, passes through the kidneys, why not *Pneumococcus?* In reference to this point, it is possible that failure to grow *Pneumococcus* from urine has been due to the fact that the organism dies out quickly in an acid medium. Should the urine be rendered alkaline, possibly results would be different.

In the mild cases studied, it was shown that during the twenty-four hours preceding improvement there was an increase in the urinary output. Chart V illustrates this to a marked degree. The case was a particularly favorable one for a test. The patient was an orderly in the hospital and was admitted on the first day of his illness. He had been famous for his earnestness in administering water to typhoid fever patients, and was responsible for the phenomenal urinary record of 25,400 cc. in twenty-four hours. When he, himself, was told to drink freely, he did so. Whether or not this was the causative factor, the fact remains that between the third and fourth days of his illness, his temperature dropped from 104.3° to 100.5°, his respiratory-rate from 35 to 24 per minute, his pulse-rate from 124 to 100, and his systolic blood-pressure from 135 mm. Hg. to normal.

It is conceivable that a large proportion of the toxic agent was thus eliminated, and that the toxic agent which remained produced phenomena similar to those which would be pro-

duced by a small dose. The temperature, respiratory and pulse curves of the chart do not return to normal until the tenth day, when, it is probable, elimination was complete or an immunity had become established. Chart I presents phenomena almost exactly similar to these; Charts II and VII, to a less degree. It is regrettable that none of the figures of the urinary output can be relied upon absolutely, but they are strongly suggestive, nevertheless, that *internal hydrotherapy* may be of the very greatest value.

Another measure, to be discussed later, which may aid

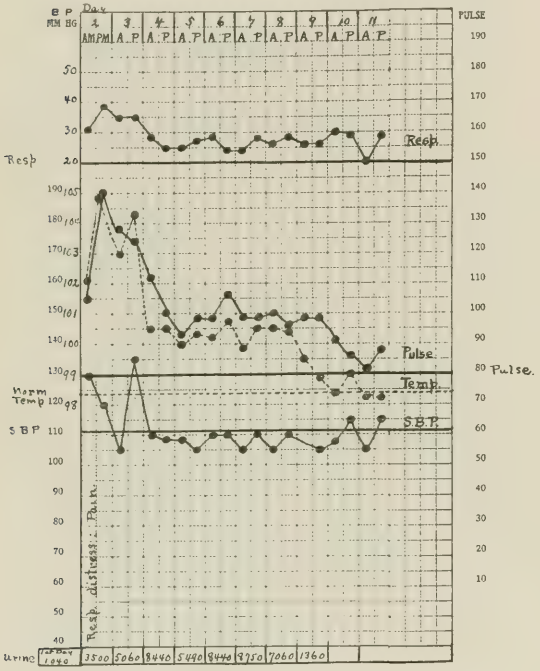


CHART V.—Linzey, male, white, age 32, heart lesion, recovery.

materially in elimination, is the administration of *digitalis*. This drug increases the urinary output through its beneficial influence upon the circulatory condition.

Amelioration of harmful influences.—Next to elimination, it is desirable to combat disturbances induced by the action of the toxic agent. Fever is met best by *external hydrotherapy;* pain may be relieved by the *ice bag* and *analgesics;* restlessness, insomnia, and delirium, by *external hydrotherapy, analgesics,* and *narcotics.* Special attention is demanded by the respiratory and circulatory conditions.

Respiration.—In accordance with the conclusions reached regarding the respiratory disturbances, it is evident that the indication is to counteract the stimulation of the respiratory center. But, if the respiratory-rate were decreased and shallow movements persisted, only a more deplorable condition would ensue. The depth of the respiration must be increased, if possible, as well as the rate slowed.

(*a*) *Heroin.*—In animal experimentation, it has been found that *heroin* in small doses reduces the respiratory-rate 30 to 50 per cent, while the depth of each movement is so greatly increased that the total volume of air respired in a unit of time is greater than before its administration. In man, *heroin* has been used to a certain extent for this action,

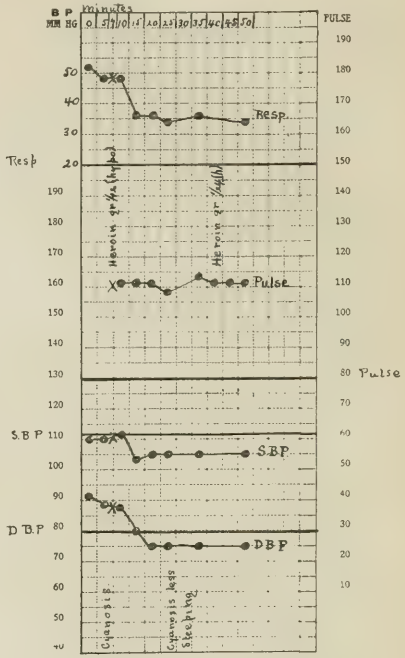


CHART VI.—Fazio, male, white, age 28.

though not nearly as much so as for its influence upon cough. If the results observed in animals could be obtained in pneumonia cases and that without untoward effects, it seemed that in this drug would be found an almost perfect physiological antidote to the toxic agent; for not only would it meet the demands of the respiratory condition, but, also it would relieve pain and cough, allay restlessness, and produce sleep.

Heroin hydrochlorate, gr. $\frac{1}{12}$, was administered hypodermically to a patient having rapid, somewhat shallow respirations (Chart VI). In eight minutes, phenomena typical of *heroin* were induced; the depth of the respiratory movements increased as the rate fell, cyanosis cleared somewhat, blood-pressure became lower, and the patient slept. One-half an

hour later, gr. $\frac{1}{24}$ was given hypodermically, and after another hour, gr. $\frac{1}{12}$, making in all gr. $\frac{1}{6}$. Following this, two more doses of gr. $\frac{1}{8}$, each, were administered hypodermically at intervals of four hours. No untoward symptoms supervened in spite of the rather large doses, and it was thought that a tolerance for the drug might be exhibited by pneumonia patients.

To the next patient, the *hydrochloride* was administered hypodermically on three successive days. The first day, gr. $\frac{1}{24}$ was given three times at half hour intervals, the results being

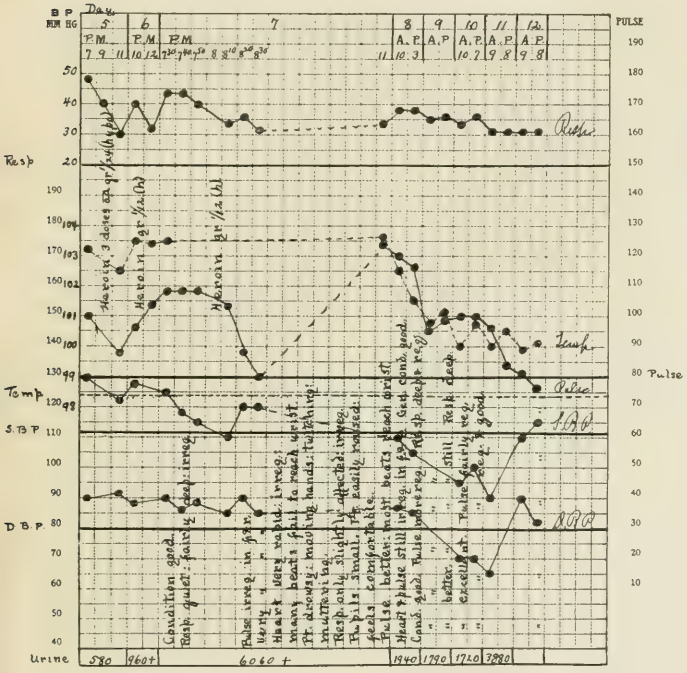


Chart VII.—Hughes, male, white, age 44, alcoholic, recovery.

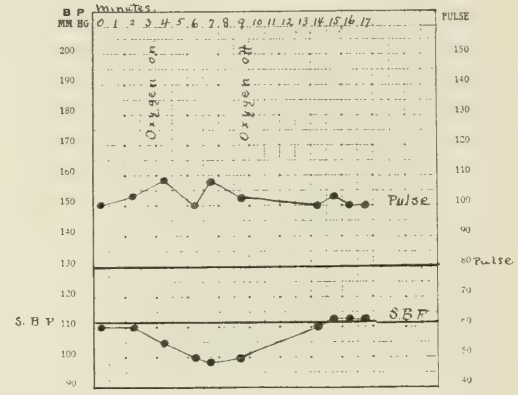


Chart VIII.

similar to those seen in the first case, though not so marked. There were no untoward effects. The second day, gr. $\frac{1}{12}$ was given in a single dose, and still there were no bad results. The third day (Chart VII, day 7), gr. $\frac{1}{12}$, again, was given. There was no respiratory insufficiency at the time. The rate became slower as before and the depth of the movements increased. But, within twenty minutes the pulse began to drop a beat occasionally, then intermissions became more frequent, and the pulse became irregular in force and rhythm. In thirty minutes after the administration, only 80 beats per minute reached the wrist, while by auscultation 132 cardiac contractions per minute were counted. The heart's action, also, was alarmingly irregular in force and rhythm, having the characteristics of so-called delirium. The respiratory condition and general condition of the patient remained good and he slept quietly, being unaware that anything was wrong. The heart improved gradually during three days until its action became regular and the heart-rate and pulse-rate equal. Recovery was good.

The condition could scarcely have been induced by depression of the cardio-inhibitory center, for section of the vagi does not affect the regularity of the cardiac rhythm, the vagus influence affecting only rate; nor was any apparent benefit derived by stimulation of the center with *digitalis*. It is probable that the untoward effect resulted from some obscure action of the drug upon the heart muscle.

In the literature that has been examined, every report in which the action of *heroin* on the cardio-vascular system is discussed states definitely that the drug has no depressing action, some observers holding that it has a favorable influence comparable to that of *morphine*. One observer finds it the best remedy that he has used in the treatment of pneumonia (5). Another reports that he has used it hypodermically in three hundred unselected cases, doses ranging between gr. $\frac{1}{12}$ and gr. $\frac{1}{4}$, and that only in the larger doses have untoward symptoms developed. These consisted of

nausea, vomiting, malaise, lassitude, and sleep (6). No mention is made of circulatory disturbances.

Considering the phenomena of the action of the toxic agent of the disease, it is difficult to believe that pneumonia renders a patient more susceptible to the action of *heroin*. Against the view are the results obtained by previous administrations, the report cited above, and the fact that in the great majority of cases the disease establishes a decided tolerance for *heroin's* parent drug, *morphine*. The patient in question had a moderate alcoholic history, and it may be that this was a predisposing factor. A third possibility seems most plausible, although one dislikes to use it, that is, the case was one of individual idiosyncrasy. At any rate, the case is sufficient to demand great care in the exhibition of the drug in pneumonia, especially in alcoholic patients. If, however, it can be shown that the disease causes no special susceptibility to the action of *heroin*, the drug should be a remedy of great value in meeting both the respiratory and general indications.

(*b*) *Morphine.*—Instead of *heroin*, should its contraindication be demonstrated, there remains *morphine*, the equal of *heroin* in every respect, except in its action upon the respiratory center. Like the former drug, *morphine* slows the respiratory-rate and deepens the movements, though it does not increase the depth sufficiently to prevent a diminution of the total volume of air respired in a given time (Cushny). But, if individual respirations are deepened sufficiently, the total volume of air entering the alveoli may be increased in spite of a decrease in the total volume respired. The table below illustrating this point is just the reverse of the previous table illustrating the progress of respiratory insufficiency.

TABLE II.

Condition	Tidal wave	Rate per min.	Total per min.	Capacity of Bron. tree	Alveolar portion of tidal wave	Rate per min.	Total per min.	%	Equivalent volume % of atmospheric *O*
1. Toxic stimulation	200 × 60 =		12,000cc.	140cc.	60 × 60 =		3600cc.	50	10.5
2. Action of morphine ..	250 × 40 =		10,000cc.	140cc.	110 × 40 =		4400cc.	61	12.8
3. Strong action of morphine.....	300 × 30 =		9,000cc.	140cc.	160 × 30 =		4800cc.	66.6	14

Condition 1 supposes respiratory insufficiency brought about through stimulation of the respiratory center by the toxic agent. In condition 2, under the action of *morphine*, the total volume of air respired in one minute is decreased 2000 cc., but the total volume entering the alveoli is increased 800 cc., bringing alveolar *O*-tension to a point equal to the tension that would be caused by an atmosphere containing 12.8 volume per cent of *O*, and respired under normal conditions. This is on the border between sufficiency and insufficiency; for, it has been said, an atmosphere containing 13 volume per cent of *O* is required, under normal conditions of respiration, to raise alveolar *O*-tension to the point of normal *O*-absorption by blood. In condition 3, the total volume is decreased 300 cc., but sufficiency is completely restored by the greater volume reaching the alveoli. Though these figures are purely hypothetical, they suggest that *morphine*, also, may be of great value in meeting respiratory indications. Moreover, as stated above, experience has shown that in pneumonia it is well borne in the majority of cases, and that, as a rule, large doses may be given without untoward effects. Like *heroin* it relieves, also, the pain, cough, and restlessness.

By consulting the charts, it may be seen that in the mild cases the respiratory-rate rarely rose above 40 per minute, while in the severe and fatal cases it ranged between 40 and 80. A rate of 40, then, appears to be upon the line of danger, and, as a working basis, efforts should be directed towards preventing an acceleration up to this point. I should suggest, therefore, the administration of *heroin* or *morphine* in small doses every two hours for a respiratory-rate of 36 or greater, the dose to be gradually increased in size until the physiological action is obtained or untoward symptoms supervene. It should be remembered, however, that the rapidity of respiration is not, after all, the factor of most importance, but that the condition of the respiratory center is best judged by the depth of respiratory movements. Therefore, during administration of the drugs, careful notes should be made regarding this point, especial attention being paid to the freedom of abdominal movements, the factor of chief value in determining respiratory depth. Any evidence that depth is not increasing with slowing of the rate should be taken as an indication to withhold the drugs.

(*c*) *Oxygen-inhalation.*—After respiratory insufficiency has become established, another measure often resorted to, but concerning the value of which there has been uncertainty, is the *inhalation of oxygen*. A patient with slight respiratory insufficiency was given *O* during a period of five minutes. Preceding, during, and following its administration, several observations on systolic blood-pressure were made and averaged. During the inhalation, a fall of 17 mm. Hg. was noted, but the pressure rose quickly to the starting point after the administration was discontinued. Another similar case exhibited the same phenomena, the fall of pressure being only 12 mm. Hg. (Chart VIII). In a third case, the fall was only 7 mm. Hg. No change in pressure was observed during observations on patients suffering no respiratory insufficiency.

Though physiology has shown that an increase of atmospheric *O*-tension above 13 volume per cent, with normal respiration, causes no increase of *O*-absorption by blood, still the phenomena are easily accounted for when it is borne in mind that in respiratory insufficiency alveolar *O*-tension is less than that produced by the above conditions. The deficient alveolar *O*-tension was increased, of course, by an increase in the quantity of atmospheric *O*. Consequently, *O*-absorption, also, was increased, asphyxial stimulation partially eliminated, and blood-pressure fell. Further effects of *O-inhalation* in insufficiency are partial clearing of cyanosis, slight slowing of the respiratory rate, and deepening of the movements. There is every evidence that the condition is partially relieved. But, following its withdrawal, insufficiency is quickly re-

established, for not only does blood-pressure rise, but cyanosis reappears, and the rate and depth of respiration return to the original point. Furthermore, it has been shown that *O* at a greater tension than normal in the atmosphere acts as an irritant upon the air passages, and that at a tension of 80 volume per cent it can produce inflammation. Considering that the air passages are in an inflamed condition already, the continuous *inhalation of O* would probably be harmful. Even during five-minute periods of administration, there is observed, almost constantly, increased restlessness on the part of the patient, who makes frequent efforts to withdraw from the *O*-cup. It is probable, then, that the partial relief of insufficiency during brief administrations is counterbalanced, at least, by the restlessness and discomfort induced, and it may be that the inflamed condition of the lungs is exaggerated by the slight irritation. Relief is partial at best, for insufficiency is due as much to accumulation of CO_2 as to deficiency of *O* in the blood, and *O-inhalation* has no tendency to increase CO_2-elimination. The weight of evidence, then, seems to point towards the probability that the measure is a useless one, at best, and may be actually harmful.

Circulation.—The circulatory condition is indirectly and favorably influenced by measures adapted to meet general and respiratory indications, and in such measures are to be placed greatest dependence. Agents used for their direct action upon the circulation are sedatives, *alcohol,* and stimulants.

(*a*) *Sedatives.*—Of *circulatory sedatives,* most important are *aconite, veratrum, hydrocyanic acid,* and the *nitrites,* all of which are known to be dangerous drugs, and with none of which have I made special observations. The sedative action of the first three, however, consists in slowing of the heart-rate through stimulation of the cardio-inhibitory center (Cushny). But all have a stimulating action upon other portions, also, of the central nervous system, excepting, perhaps, *aconite* and *veratrum* on the respiratory center, upon which their action is not understood. Furthermore, it is doubtful if stimulation of the cardio-inhibitory center by medicinal doses of these drugs would have any effect whatever upon pulse-rate in pneumonia. Stimulation of the center strong enough to overcome the excitation of the heart muscle and accelerator center would require, probably, doses of the drugs too large to be used with safety. For these reasons, all three of the drugs would be contra-indicated, a priori, in the disease.

The *nitrites* are the safest of the sedatives, and, since they act by dilating the peripheral vessels, thus lowering blood-pressure, their administration should cause a decrease in the heart's work. It is possible, therefore, that they may be of some value in preventing overwork of the heart muscle, and thus of aid in preserving the integrity of the circulation.

(*b*) *Alcohol.*—The action of *alcohol* is a matter of too great dispute to warrant its classification as either sedative or stimulant, nor would one be justified in making any dogmatic statement as to its indication. In cases having alcoholic histories and presenting the alcoholic type of the disease, it would seem reasonable to continue, as far as possible, customary conditions under which the tissues have worked. In other cases, experience has led many observers to believe that alcohol is of benefit in pneumonia; others, to the contrary view. Though I have used it and seen it used frequently, sometimes in large quantities, I have not yet made special observations on variations of respiration, pulse- and blood-pressure due to its administration, but I have never seen results, either good or bad, that I could attribute directly to its action. Abel states that moderate quantities, introduced into the circulation with the avoidance of local irritation, have no effect upon heart, blood-vessels, or blood-pressure; in larger quantities, when there is a variation, the pressure is always lowering (7). Cook and Briggs have observed, in the majority of patients in whom no tolerance was established, a slight but transient rise of systolic pressure following its administration, a phenomenon which they attribute to local irritation; and then a distinct fall of pressure, attributed to a sedative action following absorption (8). Cushny suggests that the showing of respiratory-rate and pulse-rate in fevers is due to its influence in diminishing cerebral excitement through its narcotic action. The probability is, therefore, that its administration may lessen cardiac work and nervous irritability and be of benefit during the stages of excitement. But, when enfeeblement of the respiratory or circulatory mechanisms has begun, it is probably contra-indicated. As a conservator of tissue, it is not specially indicated, since food is usually taken well, digestion is not greatly impaired, and natural products for combustion are supplied.

(*c*) *Stimulants.*—It need scarcely be argued that circulatory stimulants are contra-indicated as long as there is no insufficiency. When that condition is established, however, unless it can be relieved, it leads, presumably, to accumulation of the toxic agent, and tends towards a premature, fatal termination. The condition, it has been pointed out, is indicated by low systolic blood-pressure associated with one or more of three conditions, namely, respiratory insufficiency, a small urinary output, and signs of oncoming œdema of the lungs. In combating circulatory insufficiency it is desirable to use some remedy that will have no deleterious effect upon the central nervous system, stimulation of which, especially of the respiratory center, is to be avoided. This is difficult, for *strychnine, caffeine,* and *cocaine* owe their action upon the circulation to stimulation of the nervous system, and even members of the *digitalis* series, whose chief action is upon the cardio-vascular musculature, act as stimulants upon certain centers in the medulla. The last, however, have practically no action upon the respiratory center, and their action upon other portions of the nervous system, excepting the cardio-inhibitory and vaso-constrictor centers, is insignificant. Therefore, members of this series seem to come nearest to fulfilling the requirements, and of these the *tincture of digitalis* is probably the most reliable and efficient.

In the case represented by Chart IX, low systolic blood-

pressure was associated with both respiratory insufficiency and small urinary output, and the lungs were full of loud ronchi. During days 4, 5, and 6, *strychnine* in fairly large doses and *digitaline* (Merck's) were administered hypodermically every four hours with no rise of pressure and no relief. On the night of day 6, *digitaline* was discontinued, the dose of *strychnine* reduced, and *tincture of digitalis* ordered every four hours. Improvement of the cardio-vascular musculature was so great that, after three doses, blood-pressure rose from 105 to 150 mm. Hg. During exhibition of the drug, the urinary output was greatly increased[5] (a certain portion of the 1720 cc. of day 6 was voided during the night and after administration of the drug was begun), and by morning of day 8 the condition of the patient was improved in every respect. Blood-pressure fell, due to less intense asphyxial stimulation, before *digitalis* was discontinued, and for several days thereafter it ranged a little above normal.

[5] Erlanger and Hooker have shown that the urinary output bears no relation to variations in blood-pressure, but that it tends to vary with pulse-pressure (3). Unfortunately, no record of diastolic pressure was made, so that the effect of *digitalis* on pulse-pressure is unknown in the case. Previous to its administration the pulse was thready in character, and it is probable that *digitalis* exerted its beneficial influence by increasing pulse-pressure.

Chart X represents a case in which low systolic blood-pressure was associated with a small urinary output. Apparently there occurred an accumulation of the toxic agent which was evidenced by the onset of respiratory insufficiency and acceleration of the pulse-rate. The *tincture of digitalis* was administered every four hours during days 7 and 8, and discontinued on the morning of day 9. During days 7 and 8, before asphyxial stimulation occurred, digitalis exerted but little influence upon blood-pressure, but when respiratory insufficiency became established (day 9), cardio-vascular response was immediate and blood-pressure rose rapidly. This was due, probably, to an improved condition of the cardio-vascular musculature resulting from the action of *digitalis*. Previous impairment was indicated by the otherwise unaccountable fall of pressure preceding the commencement of its administration. In this case, also, after one day of high blood-pressure, there was great improvement in every respect in the patient's condition.[6]

The view may be held that in both of these cases the unto-

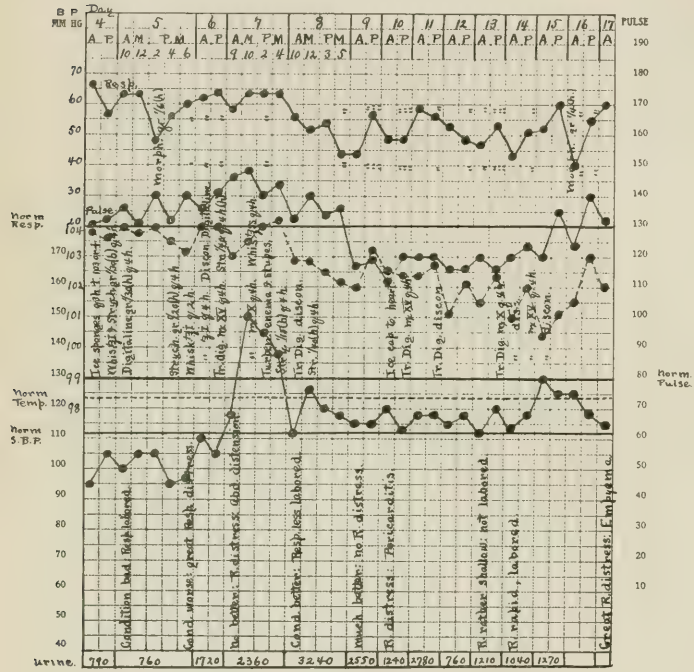


CHART IX.—Watkins, male, colored, age 16, recovery from acute illness, death from complications, empyema, and pericarditis.

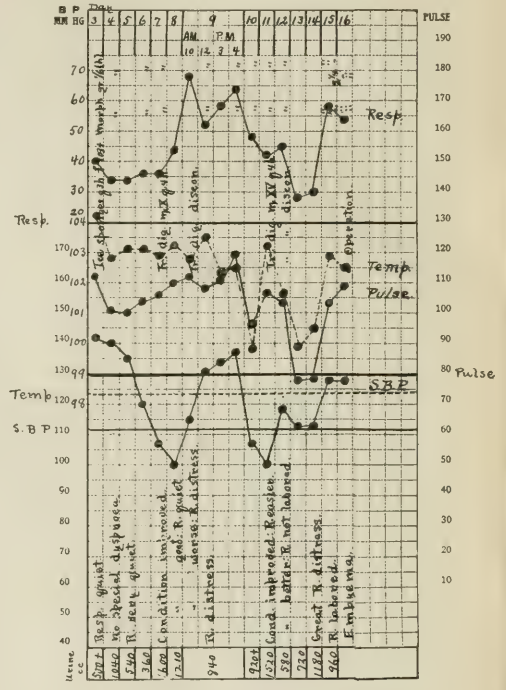


CHART X.—Clark, male, age 28, empyema, recovery.

[6] The urinary measurements are probably incorrect in this chart. A different result would certainly be anticipated during a period of improvement, and the figures here show a wide variation from those under all similar conditions in the other charts.

ward phenomena immediately following the administration of *digitalis* were due to the action of the drug. But digitalis exerts no such influence upon respiratory-rate or pulse-rate as that represented in the charts. Furthermore, in Chart IX great improvement occurred before *digitalis* was discontinued; and in Chart X, it is shown that administration of the drug in even larger doses under different conditions (days 11, 12) was associated with no similar phenomena, but with slighter rise of blood-pressure and marked lessening of the respiratory-rate and pulse-rate (day 13). The evidence, though very incomplete, seems to be in favor of the view that *digitalis* improved the circulatory condition, and thus aided efficiently in the elimination of the toxic agent, and, possibly, in its destruction through improved metabolism.

Résumé.

I. *Action of the toxic agent of lobar pneumonia.*
 1. Phenomena of the mild action bear the features of stimulation of the central nervous system and cardiac muscles.
 2. Phenomena of severe intoxication appear to result from intensified stimulation, or enfeeblement and exhaustion from overstimulation.
 3. Death occurs from (1) respiratory insufficiency terminating in asphyxiation or in exhaustion of the respiratory center, or (2) circulatory insufficiency, which leads, presumably, to accumulation of the toxic agent, and which may induce œdema of the lungs or end in exhaustion of the heart muscle.

II. *Therapeutics.*
 1. Elimination of the toxic agent.—*Internal hydrotherapy.*
 2. Amelioration of harmful influences.
 a. Fever—*external hydrotherapy;* pain—*ice bag and analgesics;* restlessness, insomnia, delirium—*external hydrotherapy, analgesics, and narcotics.*
 b. Respiratory indications.
 (1) *Heroin* or *morphine* every two hours for a respiratory-rate of 36 or greater.
 (2) *O-inhalation* is probably useless and may be harmful.
 c. Circulatory indications.
 (1) Circulatory sedatives probably contra-indicated, excepting the *nitrates,* which may be of benefit during early periods of increased cardiac work.
 (2) Alcohol indicated in alcoholic cases; may be of benefit when there is no circulatory insufficiency.
 (3) Circulatory stimulants contra-indicated, except members of the *digitalis* series. The indication is low blood-pressure associated with one or more of three conditions, namely, respiratory insufficiency, small urinary output, œdema of lungs.

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A CASE OF UNUSUALLY LARGE AORTIC ANEURYSM.[1]

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The aneurysm here reported is regarded as worthy of record, chiefly on acount of its enormous size and the presence of a collateral venous circulation.

Mr. F. R., age 60; admitted December 6, 1893; occupation, soldier; nationality, Germany.

Previous History.—No reliable family history of the patient's early life was obtained; also no history of syphilis. Patient stated that since he left the army he had been employed as a baker, and that he used to exert himself considerably at times lifting barrels of flour. He never, however, noticed any bad effects from it. Admission certificate states that he suffered with rheumatism for about three years previous to admission. He was first admitted December 6, 1893, suffering with a chronic form of mental trouble, and was discharged December 5, 1894—improved. He was re-admitted April 19, 1895 from the Central Branch, N. H. D. V. S., suffering with a recurrent attack of the same men-

[1] Presented by invitation before the Medical Society of the District of Columbia, April 26, 1905.

tal trouble. At this time the patient was a strong robust man, and showed no evidence whatever of physical debility. He remained in one of the chronic wards in good physical condition until the spring of 1903. During this period his mental condition alternated between excitement and depression, but he was never restrained or confined to bed, and at times was well enough to be given parole about the grounds.

On April 2, 1903, patient was transferred to the hospital ward, complaining of pain in the chest. This pain seemed to be worse at night, and interfered considerably with his sleep. It also aggravated his mental trouble, as he labored under the delusion that his pursuers were pumping gas into his chest. His condition remained practically unchanged until later in the summer of 1903 when in addition to the pain there was a slight cough and dyspnea, with some harshness of the voice. There appeared during September slight swelling near the right border of the sternum between the 2d and 4th costal cartilages. This pulsating expansile tumor gradually increased in size so that on November 1, 1903, it was about the size of a small lemon. It continued to grow, but the symptoms remained about the same until the spring of 1904, when they became more pronounced.

The following notes were made June 11, 1904, when the case was first seen by the writer:

Inspection.—There is a pulsating tumor 9 cm. in diameter projecting from the chest wall 6 cm. situated to the right of the mid-sternal line between the 2d and 5th costal cartilages, and extending to the right nearly as far as the nipple line. The skin over the tumor is thin, shiny and tense. There is no pulsation of the vessels of the neck, no evidence of venous compression, nor of irritation of the sympathetic; the pupils being equal, of medium size, and react readily to light. The apex beat is seen faintly in the 5th interspace 1 cm. to the left of the nipple line. There is clubbing of the fingers and slight incurving of the nails.

On *palpation* there is felt over the tumor a forcible expansile impulse of considerable resistance. There is a marked diastolic shock and systolic impulse. The apex beat is feeble.

Percussion.—Area of cardiac dullness is slightly increased. The note over the tumor and for a small area surrounding it is flat. This flatness blends with the cardiac dullness to the left.

On *auscultation* no bruit can be heard. The only adventitious sound present is a loud creaking sound heard on inspiration in the right infraclavicular space. There are no valvular murmurs, but the second aortic sound is markedly accentuated. About every 15 or 20 beats there is absence of the first sound. There is no appreciable difference in time between the right and left radial pulses, but the right is very much weaker than the left. There is no tracheal tugging.

The patient complains of continued dull pain, with occasional sharp lancinating attacks felt most distinctly in the right axilla and along the right arm. There is occasional slight cough, considerable dyspnea, and the voice is quite husky. As near as can be made out the 3d and 4th costal cartilages are eroded, as well as a few cm. of the 3d and 4th ribs.

The tumor from about this time increased in size with remarkable rapidity. There was noticed about August 1, 1904, enlargement of the superficial veins of the right half of the body. These veins rapidly became more dilated and tortuous, the flow being from above downward. The veins entering into this collateral circulation, were in the order of their size, the right superficial epigastric, a large branch from the left superficial epigastric joining it near the umbilicus, several lateral thoracic veins, the right jugular and a network of superficial veins over the tumor, and over the superior and anterior surfaces of the right shoulder. This collateral venous circulation was thought to be due to pressure on the right innominate vein, and perhaps also slightly on the superior vena cava.

There appeared during September, in addition to the symptoms above mentioned, well marked tracheal tugging, and also an area of softening about 5 cm. in diameter at the summit of the tumor. This area was discolored, but at no time was there any weeping or leakage of blood.

The dyspnea and pain became quite distressing during October, and on the 23d of that month a sudden change occurred. The dyspnea became markedly increased, the extremities were cyanosed, the temperature rose from normal to 100 degrees, pulse from 82 to 110 and quite feeble, and the respiration from 22 to 28 per minute. The next day this condition was somewhat improved, but he gradually grew weaker during the succeeding 21 days and death occurred November 13, 1904, at 8:58 a. m. For a few minutes preceding death the pulse fell to 13 and the respiration to 4 per minute.

Autopsy Notes.—(Case came to autopsy in the service of Dr. I. W. Blackburn.)

Autopsy performed at 1.50 p. m., November 13, 1904, five hours after death. The body is that of a medium size, well built, and well nourished white man. It is slightly warm, and there is no post-mortem rigidity, and very slight cadaveric lividity. The pupils are equal. There are no scars on the genital organs or elsewhere. The superficial veins of the right half of the trunk are somewhat dilated and tortuous, especially the right superficial epigastric. There is a tumor of the following dimensions occupying the space between the mid-sternal line and the axilla, and the 2d and 7th ribs on the right side, H 30 cm., V 23¾ cm., C 65 cm. The skin over the tumor is smooth and shiny. It is somewhat soft to the touch over its entire extent, but more markedly so over an area about 5 cm. in diameter at the summit. There is some edema of the right arm and tissues adjacent to the tumor.

The aneurysm with heart, lungs, and a large portion of chest wall are removed en masse by the following incisions: an incision in the left mammary line extending from the clavicle to the costal margin; another the entire length of the right posterior axillary line—their ends being joined by an incision along the costal margin, and one along the superior opening of the thorax —the sternal ends of the clavicles being disarticulated.

Fluid blood flows freely from the great vessels.

Pericardium.—There are many old fibrous adhesions between the pericardium and pleura; otherwise it appears normal.

Heart and Aneurysm.—There is apparently no cardiac hypertrophy. In order to preserve the specimen intact the heart is not detached, but the aortic arch is opened by an incision begin-



FIG. 1.—Taken 5½ months before death.



FIG. 3.—Taken the day before death.

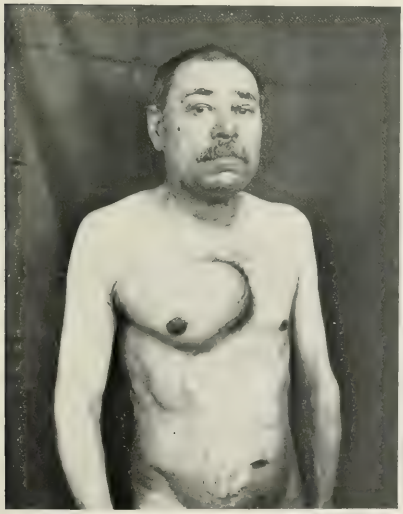


FIG. 2.—Taken 45 days before death, showing collateral circulation.



FIG. 4.—Taken the day before death, showing the lateral extent of the aneurysm and the area of softening of the skin over the most prominent point.

ing just above the valves at the anterior-left-lateral border and keeping this same relation all the way around. The aortic arch is much dilated and shows numerous atheromatous patches; many of the calcareous plates protrude into the lumen of the vessel. The greatest dilatation is between the valves and the origin of the innominate artery and is large enough to readily admit the closed fist. Through the right wall of this sac is an oval opening 8 cm. in its long diameter, its lower margin being 6 cm. above the aortic valve. This opens into an enormous sac which occupies the greater part of the right half of the chest. This sac is opened, after the adherent right lung is dissected away, by an incision along its posterior superior border. This sac contains, after the fluid blood is drained off, 2200 grams of clot. 1520 grams of this is from the extra-thoracic portion of the sac, and is light brown in color, rather firm, laminated and adherent to the sac wall. The remaining 680 grams from the intra-thoracic portion of the sac is more recent, darker and quite soft. The intra-thoracic portion of the sac is not nearly filled with clot, as it was from this part that most of the fluid blood escaped. There is seen an area of atrophy of the sac wall about 6 cm. in diameter at the posterior-superior portion near the median line. This had permitted oozing of blood into the anterior-inferior portion of the upper lobe of the right lung, and the formation at this point of a clot about the size of a small lemon.

The sac protrudes through the chest wall between the 3d and 5th ribs. The 3d rib is eroded along its inferior border about ⅓ of its width, beginning 7½ cm. from the edge of the sternum. The 4th rib is completely eroded for a distance of 12 cm., beginning 6¾ cm. from the edge of the sternum. An irregular fragment of this rib 6 cm. in length is found loose in the extra-thoracic sac. The cartilage of the 5th rib is broken 2½ cm. from the sternum, and the rib is displaced forward and slightly downward. Its superior border is eroded to about the same extent as is the inferior border of the 3d, beginning the same distance from the sternum. This opening measures H 12 cm., V 9 cm. The aortic valves are slightly thickened, but not calcareous and appear to be competent. The other valves, the coronaries and myocardium, are not examined as it is desired to preserve the specimen intact. The lower portion of the thoracic, aorta, and the abdominal aorta show nothing abnormal.

Pleuræ.—The pleuræ are thickened, and there are numerous fibrous adhesions between them and the pericardium and diaphragm.

Lungs.—These organs are necessarily much mutilated in removal. The left lung is œdematous, but shows no other abnormality. The right lung shows marked compression, and the clot mentioned above.

Spleen.—200 grams; abnormally firm and full of blood.

Kidneys.—170 grams each. Capsules are readily removed; the surfaces are a little glandular.

Liver.—1390 grams; apparently normal. Gall-bladder contains 40 cc. of orange-colored bile.

Intestines.—Excepting a constriction in the sigmoid flexure admitting only the index finger, the intestines appear normal.

Pancreas.—Apparently normal.

Brain.—1100 grams. The membranes show considerable opacity and there is general shrinkage of the convolutions. The vessels show little patches of opacity, but no calcareous change. Otherwise there is nothing abnormal to be noted.

Skull.—Rather thin. Frontal suture is persistent.

Autopsy closed at 4 p. m.

Adopting the view that a true aneurysm is one consisting of one or more of the coats of the vessel, it is difficult to say just how much of this aneurysm is true and how much false. We can state with a fair degree of certainty that the intima and media ended at the opening in the dilated aortic arch, and that the adventitia became very much distended. It was impossible to determine the extent of this distention, owing to the new formation of fibrous tissue, but it is hardly likely that it extended beyond the opening in the chest wall. Perhaps the greatest pressure on the sac was exerted at this point and produced rupture of the adventitia. This supposition would make all of the extra-thoracic portion of the sac purely false.

It is difficult to demonstrate, without serious injury to the specimen, the exact site of venous compression which produced the collateral circulation. Apparently the greatest pressure was exerted on the superior vena cava and the right innominate vein was probably pressed upward against the clavicle. Another possible explanation of obstruction to the flow of blood in the innominate vein is that, as the superior vena cava was pressed toward the left, it may have caused some angulation of the innominate.

The cause of the sudden change in the patient's condition on October 23 was thought to be due to the hemorrhage into the right lung.

Another point of interest in this case is the influence the physical disease appeared to have upon the mental condition. Although the patient was adjudged to be of unsound mind for a period of nearly ten years, there is no history of such well marked delusions and such vivid hallucinations as were manifest during the last seven or eight months of his life. Every morning he would complain of the way "they" treated him during the night with their electric wires and gas pipes. He believed that they pumped gas into his chest, and that this accounted for the swelling, pain, and difficulty in breathing. He begged to have the tumor opened to let the gas out, or to have a poultice applied, or a salve or leeches put on. He threatened to open it himself, and had to be closely guarded to prevent such threats from being carried into execution. The hallucinations were entirely auditory. He would hear the voices of his persecutors day and night, and would scream back in answer to them, using much profanity and abuse.

These mental symptoms grew more and more pronounced until within about three weeks of his death when they subsided somewhat. They were, however, well marked even to the end, but owing to his weak and exhausted condition they were not so apparent, as he could no longer jump out of bed, nor talk so loud as he had done previously. The patient manifested no other mental symptoms of interest. There was a fairly well marked degree of dementia.

We see therefore a connection between the mental symptoms and the physical disease, reminding us of cases occasionally met with in the literature of misinterpreted sensations and other mental phenomena occurring in various visceral diseases. I refer particularly to the observations of Dr. Henry Head, Brain, 1901, and Dr. Carey B. Gamble, Johns Hopkins Bulletin, July and August, 1904.

I wish to state that I am indebted to Dr. I. W. Blackburn for useful suggestions and supervision of the preparation of the specimen, and to Dr. H. J. Nichols for assistance with the making of a plaster cast and the photographs.

ACUTE PERICARDITIS COMPLICATING ACUTE LOBAR PNEUMONIA.[1]

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During the period of sixteen years, viz. from May 15, 1889, to May 15, 1905, 665 patients suffering from acute lobar pneumonia have been admitted to the Johns Hopkins Hospital. These figures include all cases, both those admitted with the disease and those developing terminal pneumonias.

Acute pericarditis was present in 31 patients, or 4.66 per cent. In 13 or 41.9 per cent, pericarditis was recognized during life; in the remaining 18 patients it was only recognized at autopsy. Autopsies made in 26 instances confirmed the diagnosis of acute pericarditis or showed its presence when not suspected before death. The analysis of the cases is as follows:

Age.—The average age of the patients was 32.5 years. The complication occurs more frequently in young adults, only 5 patients out of the last 19 in this series being above the average age (32.5 years) and the majority were much younger.

Sex.—There were 22 males and 9 females. Of the males 10 were white and 12 colored; among the females 5 were white and 4 were colored.

Duration.—The duration of the illness being so indefinite and in many cases unobtainable, I have merely considered the time the patient was in the hospital, which in most instances was quite short. In 2 patients, however, it was long, due to a protracted illness of another nature (arthritis deformans and typhoid fever) in a third patient the development of an empyema caused much prolongation of the disease. The remaining 28 patients showed an average duration of 6 days.

Lung Involvement.—The portions of the lungs involved during the disease were as follows:

Right side	Times	Left side	Times
Upper lobe	2	Upper lobe	0
Lower lobe	1	Lower lobe	2
Upper and middle lobes	2	..	..
Upper and lower lobes	2	..	..
Middle and lower lobes	1	..	..
All lobes	5	Both lobes	3
Total	13	Total	5

The lungs on both sides of the chest were involved at the same time in 13 patients, the distribution of consolidation being as follows:

Right side	Left side	Times
Right lower lobe	and left lower lobe	2
All lobes	and left lower lobe	3
Right lower and left upper and lower lobe		2
Right lower and middle and left upper lobe		1
Right lower and middle and left lower lobe		1
Right upper and lower and left lower lobe		1
Right upper and lower and left upper and lower lobe		1
Right upper and left lower lobe		1
Right upper and left upper and lower lobe		1
Total		13

Heart condition.—In regard to the recognition of the pericarditis during life it may be said that in 12 instances there was no note of any pericardial rub, or other symptoms to indicate a pericarditis. In 13 patients pericarditis was diagnosed. Five cases were doubtful; in one the patient was too restless and delirious for a satisfactory examination. Of the remaining four, the sounds in the lungs were so loud, that the heart condition was masked, though in one instance a suspicious rub was heard over the heart, but it was not sufficiently plain to justify a diagnosis of pericarditis. In the sixth doubtful case there was no note of any pericardial rub, but the increase of cardiac dullness to the right of the sternum was suggestive of an effusion into the pericardium and the autopsy in this case showed some excess of fluid.

Complications.—In the clinical histories pleurisy was by far the most common complication, occurring as follows:

Acute fibrinous pleurisy, right side, 7 cases; left side, 7 cases; both sides, 2 cases; pleurisy with effusion; right side, 1 case; left side, 1 case. The other complications were empyema 3 times; acute nephritis, acute endocarditis, and pneumothorax once each. Of the associated diseases, typhoid fever, arthritis deformans and acute articular rheumatism occurred once each, the pneumonia having developed during their course.

Mortality.—The mortality was extremely high, 29 patients out of the 31 dying, or about 93.5 per cent.

Remarks.—A marked history of alcoholism was given by 10 patients. Occupation had little bearing on the disease, the majority being laborers as in most hospital series. Two patients gave a history of previous attacks of pneumonia. Another had had both pneumonia and acute rheumatic fever previously and one other acute rheumatic fever only. Two patients showed a general pneumococcus infection, the organism being cultivated from the blood during life. Four cases were admitted in active delirium and two became delirious during the course of the disease—delirium therefore occurring in 19.3 per cent. There were two instances of terminal

[1] Read before the Johns Hopkins Hospital Medical Society, June 5, 1905.

pneumonia or 6.45 per cent. This small percentage is rather interesting as we know what a fatal complication pericarditis is and how often it is a feature of terminal infections in other cases. It does not seem so common in terminal pneumonia, judging from the small number of cases found here.

The Autopsy Records.—As so many of the fatal cases come to autopsy, their pathological and bacteriological findings should be reviewed, especially because in many no definite diagnosis could be made before death. During the past sixteen years 184 autopsies have been made at the hospital on cases of acute lobar pneumonia; among these there were 29 cases, or 15.7% with acute pericarditis, 26 of which are noted above, the other three having no clinical histories.

Lung Involvement.—In analysing these cases we find the lung involved as follows, according to lobes consolidated:

Right side	Times	Left side	Times
Right upper	2	Left upper	0
Right lower	1	Left lower	2
Right upper and lower	1		
Right upper and middle	2		
Right lower and middle	1		
All lobes	7	Both lobes	2
Total	14	Total	4

In combination both sides of the chest were involved together in 11 cases as follows:

Right side	Left side	Times
Right upper and	left lower	2
Right upper and	both left lobes	2
All right lobes and	left lower	2
All right lobes and	both left lobes	1
Right middle and lower and	left lower	1
Right middle and lower and	left upper	1
Right upper and lower and	left upper and lower	1
Right lower and	left lower	1
		11

Pericarditis.—The varieties of pericarditis were as follows in order of frequency.

Acute fibrino-purulent pericarditis	10 times.
Acute sero-fibrinous pericarditis	9 "
Acute fibrinous pericarditis	8 "
Acute purulent pericarditis	2 "

In 3 instances only, was a very large amount of fluid present. In two patients, one with 500 cc. and the other with 800 cc. of fluid, the clinical history was not obtainable, so the question as to whether the pericardial effusion was diagnosed before death cannot be answered. The third patient had 1000 cc. of fluid, but the associated empyema on the left side interfered with the recognition of the pericardial effusion and it was only discovered at autopsy.

Bacteriology.—In regard to the organisms cultivated and recognized, the presence of the pneumococcus only, when found, is tabulated, thus:

Lungs.—The pneumococcus was obtained in culture in 16 instances and found microscopically in cover-slip smears made at autopsy 7 times when the cultures were negative, a total of 23 in 29 autopsies. From the *pericardium* the pneumococcus was cultivated 12 times and the smears showed its presence in 7 other cases. Consequently, in 19 of the 29 cases of pericarditis the pneumococcus was the organism present. No other important organisms were cultivated, in most instances the cultures or smears being sterile or contaminated.

Bacteriological findings elsewhere in the body were as follows:

Heart's blood pneumococcus cultivated	5 times.
Pleural exudate pneumococcus cultivated	3 "
Empyema pneumococcus cultivated	2 "
Lung abscess pneumococcus cultivated	2 "
Mitral valve pneumococcus cultivated	1 time.
Brain pneumococcus cultivated	1 "

Complications.—Pleurisy was so frequent as to be regarded as more than a complication, being present in 28 of the 29 autopsies. The sides involved were as follows: right side, 13 times alone; left side, 8 times alone; both sides at same time in 7 instances. Pleurisy with effusion occurred 12 times. Empyema was found 3 times, twice on the right side, both of them being encapsulated between the diaphragm and lungs. In the third case the empyema was on the left side, not encapsulated. Abscess of the lung occurred twice and acute purulent meningitis and acute mitral endocarditis once each. Acute mediastinitis was present in a number of cases, its frequency being hard to determine exactly, as often no note of its presence or absence was given in the records.

Remarks.—In looking over both the clinical and pathological records, one is especially struck with the seriousness of pericarditis in acute lobar pneumonia. It is hard to say whether the cases of pneumonia, in which pericarditis occurred, were any more severe than usual or whether pericarditis is only one of the many manifestations which develop at the end of a severe pneumonia. A striking fact in the records is the more frequent involvement of the lung and pleura on the right side. This would seem to indicate that pericarditis is due to a metastatic process, through the blood or lymphatics rather than by direct extension from the lung or pleura. This is of interest in the light of the fact that great stress has been laid by many in previous reports on the synchronous involvement of the left lung and pleura, which as we know envelops the heart more than on the right side.

In the autopsy records, I found a case of a woman who had a large hemorrhagic infarct in the upper right lobe of her lung, the pleural surfaces over this area showing fresh fibrinous adhesions; a fresh sero-fibrinous pericarditis was also present. The lung and pleura were otherwise not involved, yet the cultures from the infarct and pericardium showed the presence of the pneumococcus. This case seems strongly to favor the view of an infection by the blood stream or lymphatics rather than by direct extension.

Recent work also shows how often the pneumococcus can be cultivated from the circulation, or other pneumococcic processes outside of the lung involved. The great frequency of pleurisy may be of some importance in explaining the extension of the disease, but granting this, the right side has

been found involved more than the left, the pleural surface of which (*i. e.* left) is much more in contact with the pericardium.

The prognosis of pericarditis complicating acute pneumonia, to judge from our own cases and the general statistics in the literature, is exceedingly grave. Our two cases of recovery were of interest, owing to the fact that both were associated with another disease; one, a white male, age 43 years, who was admitted for treatment of arthritis deformans and spondylitis, was in the hospital 237 days. After admission he had pneumonia involving the right and left lower lobes lasting several weeks; during its course a definite pericardial rub was heard for several days. There was no active arthritis at any time to suggest a rheumatic pericarditis; later the patient left the hospital much improved. The other instance of recovery was a white female, age 29 years, who was admitted with all the signs of pneumonia, with involvement of the right upper and lower and left lower lobes. A pericardial rub was present on admission and lasted several days. Later the patient had an attack of fever, with positive Widal reaction, rose spots, and an enlarged spleen; after remaining in the hospital 119 days she was discharged quite well.

The treatment of patients in whom the pericardial rub was recognized during life, was of the general supportive character, usually employed in pericarditis. Locally ice-bags and blistering were tried. All treatment except in the cases of two who recovered seemed to be unavailing.

In no instances was aspiration or free drainage tried.

Literature.—Upon a review of the literature bearing on pericarditis as a complication of pneumonia, opinions are found to vary somewhat as regards its frequency, mode of infection and mortality. Most writers however agree as to its seriousness, thus:

Fowler and Godlee[1] found pericarditis 17 times in 128 fatal cases of pneumonia or 13.2%. They say: "It is generally stated that this complication (pericarditis) is more frequent in cases of pneumonia in which a portion of the left lung in contact with the pericardium is consolidated, but in these fatal cases the right lung was involved 10 times, the left 6, and both lungs once."

Our statistics seem to agree quite closely with theirs.

Pye-Smith[2] says: "Pericarditis is not infrequent and is an extremely dangerous complication. Double pneumonia with pericarditis is almost invariably fatal. * * * "Pericarditis follows more particularly when the pneumonia or pleurisy is on the left side. In 434 cases of pneumonia, pericarditis was present in 14, all fatal."

A. H. Smith[3] says: "This complication (pericarditis) occurs in 2 to 8% of the cases of pneumonia, according to different authorities. At the Presbyterian Hospital, N. Y., it was made out during life in 6 out of 485 cases of pneumonia, about 1.2%."

Strümpell[4] in speaking of the complications of pneumonia, after mentioning pleurisy, says: "Still worse is a sero-fibrinous or purulent pericarditis, which in not very rare instances, is revealed at autopsy as the special cause of death. We must note however that recovery sometimes takes place in spite of an empyema or a purulent pericarditis."

Osler[5] found pericarditis present in 5 of his 100 autopsies.

In their book on Pneumonia, *Sturges and Coupland*[6] say: "Pericarditis is an interesting and serious complication and in many instances its presence is not declared during life. It is mostly described as more common in association with pneumonia and pleurisy of the left side (this statement made on the authority of Bouillard) and hence may be regarded as due to a direct extension of the inflammatory process to the pericardium. But in an analysis of 144 autopsies (Middlesex Hospital, 1873-1889) this is by no means the rule, for out of 24 cases of acute pericarditis, in no fewer than 11 was the right lung involved, in 10 the left and in 3 both lungs. It may be remembered however that pericarditis was more frequently combined with pleurisy of the left side."

"In 23 cases of pericarditis and pneumonia coexisting, the right lung was consolidated in 16 either solely, which was the rule or with very slight consolidation of the left; of the remaining 7 cases, 4 were not distinctive." Among some statistics they quote are the following: "Leudet met 6 cases of pericarditis out of 83 pneumonias. Austin Flint 8 out of 133 cases. Behier 3 out of 114 cases of pneumonia. Huss in his 2616 cases of pneumonia gives 22 cases of pericarditis, 12 of which were fatal."

Babcock[7] says: "Acute lobar pneumonia should certainly be given a place only subordinate to acute articular rheumatism, in the etiology of pericarditis." He quotes Preble as having found pericarditis in 92.4% of 79 fatal cases of pneumonia collected from the post-mortem records of the Cook County Hospital, Chicago. Preble came to the conclusion that the danger of pericarditis bears a distinct relation to the extent of lung involvement and is also more frequent in left than right-sided pneumonias.

McCrae, Fyshe and *Ainley*[8] in an analysis of 486 cases of pneumonia and 100 autopsies, found pericarditis in 11 cases, about 2.3%, (ours 4.66%) whereas the analysis of the autopsies gave a percentage of 17%, (ours 15.7%). "The discrepancy that exists between the clinical and pathological records is easily understood when one remembers the comparatively short time in which a pericardial friction rub may be present and the small amount of fluid present in many cases." "Of their cases 7 occurred with involvement of both lungs, 5 of the right side and 4 of the left."

Anders[9] found acute pericarditis 14 times in 275 cases of pneumonia, about 5%, and *Geo. W. Norris*[10] in 500 cases of pneumonia in the Pennsylvania Hospital (1897-1901), found acute pericarditis as a complication in 4 cases, 3 of which were fatal.

J. A. Scott[11] reports and discusses an interesting case of purulent pericarditis secondary to pneumonia with operation and recovery. In cases where fluid is suspected, free drainage even in desperate cases may give favorable results at times. One of our cases which might have yielded better results with aspiration and free drainage, was the one mentioned with a large pericardial effusion (1000 cc.), but

the accompanying left-sided empyema masked the pericardial condition.

John B. Roberts[12] has an interesting article in the Amer. Jr. Med. Sciences for December, 1897, on the surgical treatment of suppurative pericarditis; and *Morris Manges*[13] says: "There have been 6 cases of pericarditis in the Mt. Sinai Hospital, N. Y., 3 recovered and 3 died. Aspiration did good in all but one case of a boy with double pneumonia and purulent pericarditis, who recovered in 38 days after aspirating, opening and drainage of the pericardium. *Skoda's* two rules for entering the pericardial sac are given: (1) Distension with a large exudate, showing no tendency to absorption and the patient getting worse, and (2) a vital indication is intense dyspnea.

Among the French are found the following statistics:

Netter[14] says: "Lesions of the pericardium are not at all exceptional; they are analogous to those of the pleura with which they often coexist."

"It varies with the different years and the severity of the pneumonia, thus we note its frequency in 1804-05, again in 1837, '76, '82, '86, and 1890. In our series pericarditis was most common in 1900, there being 6 cases. As to statistics, Netter says: "Ormerod found pericarditis 12 times in 100 pneumonias, Leudet 6 in 83 cases and Grissole 3 times in 58 cases of pneumonia."

Vignau[15] collecting and combining various statistics, believes that it occurs in from 5 to 8%.

Laudouzy[16] says: "Pericarditis was observed in 8% of Netter's cases. Rarely is it accompanied by an abundant effusion and coexists often with other pneumococcic manifestations as meningitis, endocarditis, etc." *P. Merklen*[17] says: "Bouillard considers the complication (pericarditis) as common, others only in 1 to 2% of cases."

Among the German statistics, *Sello*[18] reports upon 750 cases of pneumonia, in which he found pericarditis in 7 cases, or about 0.9%; 5 died and 2 recovered. In 4 purulent cases, the right lung was involved in 3 and the left only once. Sello reports other men as finding this complication as follows; von Jürgensen in 0.5%, Fismer in 3.9% and Rychner in 2.7%.

To illustrate the more frequent involvement of the right lung *John L. Steven*[19] found pericarditis 13 times in 120 fatal cases of pneumonia; the right lung being involved in 8 cases. Left in 3 cases and both lungs in 2 cases.

John Hay[20] reports in the Lancet on 200 cases of acute lobar pneumonia. He found 9 cases of pericarditis, 6 of which were fatal; he says: "I found it to be a most serious complication, probably because it is so potent in damaging the myocardium, also from the fact that it is sometimes merely a terminal event in a severe case or again it may be and I believe, is, frequently, a symptom of its severity."

In a report of 28 cases of suppurative pericarditis in children, *George F. Stille*[21] found that 11 gave positive cultures of pneumococci, of the rest, although no bacteriological examination was made of the pericardial fluid, yet the other associated lesions, empyema or pleurisy following a pneumonia, yielded pneumococci.

Sears and Larrabee's report[22] of 949 cases of pneumonia I wish to give somewhat in detail because our observations seem to agree fairly closely with theirs. "The recognized difficulty of diagnosing pericarditis in the presence of pneumonia received a further illustration in these cases, since only about half were discovered during life, and in some of these, which were represented only by a friction rub, the inflammation may have been outside and not within the pericardial sac, yet the number that was found at autopsy, shows that it is not a very rare complication, at least among the fatal cases, since it was found in 8 of 72 autopsies. Out of 19 cases in which it was diagnosed, 11 died; in some of which it was simply an incident in a general pneumococcus septicemia. In 5 only a considerable amount of fluid was present and in 3 was there sufficient to have embarrassed the heart."

"It occurred more frequently when the right lung alone was attacked, for in 10 of 18 cases in which there were complete data, it was confined to that side. The distribution of lung involved being as follows: Right upper, 3 cases; right lower, 2 cases; whole right lung, 3 cases; left upper lobe, 1 case; left lower, 1 case; whole left lung, 1 case. The following combinations of both lungs occurred *once* each whole left lung, with right lower; whole left lung, right middle; whole right lung, with left lower; right upper and lower and left lower; right middle and lower and left lower; right upper and middle, and left lower; and right and left lower once. Acute mediastinitis was found 3 times at autopsy."

Finally *F. P. Henry*[23] reports upon the clinical and pathological findings in a case of pneumonia of the left side with purulent pericarditis and says: "A study of this case has convinced me that the diagnosis of pericardial effusion complicating left-sided pneumonia, is to be made, as much by the symptom, (cyanosis, rapid pulse and dyspnea) as by the physical signs."

Conclusion.—It may be said that pericarditis developing during the course of an acute lobar pneumonia, is a most serious and important complication occurring more especially in young adults, frequently insidious, latent, and often not recognized during life.

It appears to arise as frequently by a metastatic process as by direct extension.

Treatment is very unsatisfactory and often unavailing, except when fluid is present in which case it is more surgical than medical.

In all patients with pneumonia, a most careful watch should be kept on the heart, as this complication appears to be much more frequent than is generally supposed, and urgent treatment in the early stages may materially reduce a high mortality.

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THE RISE OF THE PRESENT CONCEPTIONS AS TO THE CAUSE OF THE HEAT-BEAT.

I. Early Ideas, and the Neurogenic Theory.[1]

By E. G. Martin.

About the middle of the eighteenth century Haller gathered together in his great work, The Elements of Physiology, all the known physiological facts and all the accepted physiological theories of his time. Although his presentation of the various theories was undoubtedly influenced somewhat by his own views, there is no reason to suppose that the thought of his time is not truly represented. All works on general physiology since the time of Haller refer constantly to him, and in the first half of the nineteenth century, particularly, all theoretical points were discussed with reference to his views, either upholding his standpoint or opposing it. For this reason, it seems to me, no better starting point can be found for a review of the growth of a theory in modern times than his work offers. I have chosen, therefore, to begin this study with an account of the facts regarding the heart-beat which were known to Haller, together with his interpretation of them.

In addition to the general facts of the heart's action, which had been known since the time of Harvey, Haller was in possession of a few special facts. These were, first, that the excised heart of a frog continues to beat for a considerable time after removal from the body, second, the results of some experiments performed by himself. In these experiments, performed upon mammals, he cut the venæ cavæ so that no blood could enter the right auricle. He observed that this chamber, thus emptied of blood, promptly ceased to beat, although the other parts of the organ continued to contract as usual. Haller concluded that inasmuch as the heart continues to beat after removal from the body, it must contain within its own substance, independently of its nervous or other connections, the property of irritability. By the term "irritability" Haller meant the ability to respond to stimulation by contraction. He supposed that this property was possessed by the heart to a very high degree, much higher, in fact, than was exhibited by any other of the bodily tissues. He supposed that the heart was excited to contract normally by the blood flowing through it, being led to this conclusion by this observation that a chamber of the heart came to rest when its blood supply was cut off. He thought that in the case of the excised heart of the frog, the stimulus for the long continued activity was furnished by the bubble of air which was enclosed within it. He had made the observation that the inner surface of the muscular wall of the heart is much more sensitive to stimulation than the outer surface.

For more than fifty years after Haller's time, his explanations of the cause of the heart-beat appears to have received general acceptance.

At any rate it was not until the end of the first decade of the nineteenth century that his views were called in question. Physiologists had been sufficiently active in other directions during this half-century, but it was not until the time of which I am speaking that their attention was directed again to this particular field of inquiry. The work which had the effect of exciting interest at this time in the cause of the heart-beat, because of the complete refutation of Haller's views it seemed to contain, was that of the French neurologist and physiologist, Legallois, a brief account of whose life, I wish now to give.

Cesar Julien Jean Legallois was born in a little village of Bretagne in 1770. After completing his elementary studies, he entered upon the study of medicine at Caen. He was still in this place when the Revolution broke out, and when, in 1793, on account of the proscription of the Girondins, the provinces rose in insurrection against the Convention, he joined in the uprising. He was denounced, was obliged to conceal himself, and sought a refuge among the medical students in the Paris hospitals. Here he was found out and denounced a second time. This time, how-

[1] Read before the Physiological Seminary of the Johns Hopkins University, February 24, 1904.

ever, instead of attempting to escape, the young student presented himself before the Committee on saltpeter and gunpowder, submitted to a severe examination, and proved that he could be useful to the Committee. The outcome was that instead of suffering punishment as an insurrectionist, he was sent to his department to direct the manufacture of gunpowder there. Upon the foundation of the School of Hygiene a year later, Legallois was entered as pupil from his district. He distinguished himself at this school, combining the study of medicine with that of ancient and modern languages, and pursuing both with success. He received his doctor's degree in 1801. With the beginning of his active life work as a physician, began also his career as a scientific investigator. During the twelve succeeding years he carried on a number of researches, chiefly upon the functions of the spinal cord. In the year 1813 he was appointed physician at the Bicêtre, a hospital about five miles south of Paris. It was his custom to make the trip each day, between Paris and the hospital, on foot. On one of these journeys he contracted a pneumonia which, according to his biographer, M. Boisseau, killed him because he refused to be bled, believing that his malady was one of depleted vitality, which did not require that treatment. This same biographer speaks of him thus: "He was an experimental physiologist of the highest order, characterized especially by the inventiveness and skill with which his experiments were carried out, and by his conservatism in drawing conclusions." Flourens says of him: "Legallois, who knew neither the prestige of eloquence, nor the easy success which arises through the influence of friends, modest precurser of the modern science of the nervous system, died at his post, not having obtained the renown which should, in justice, have been his."

The experiments of Legallois which bear upon the question of the cause of the heart-beat, and with which, therefore, we are concerned at this time, appeared in the year 1812 in a publication entitled: "Experiments on the principle of life and particularly on the principle of the motion of the heart, and on the seat of this principle." An American translation appeared the following year in Philadelphia. Legallois' experiment was a simple one. He crushed the spinal cord of a rabbit suddenly, and observed that the heart stopped beating. His conclusion from this experiment was that whatever might be the case in the frog, in the rabbit the heart is dependent, for its power to contract, upon the spinal cord. In other words, he concluded that the origin of the beat of the mammalian heart is neurogenic.

In the year 1810, Sir Benjamin Brodie delivered the Croonian lecture before the Royal Society. His subject was: "On the influence of the Brain on the action of the Heart, and the generation of Animal Heat." This was two years before the appearance of Legallois' paper, and while there is no reason to suppose that Brodie knew anything about the work of the French investigator, it is certainly an interesting coincidence that these workers should have hit upon such similar lines so nearly at the same time. It is equally interesting that they reached conclusions diametrically opposed to each other. The work of Brodie, to be sure, had to do with the brain, and that of Legallois with the cord. Brodie reported that he could cut the head off a dog or rabbit and if artificial respiration were established promptly, the heart would keep on beating normally. He concluded that the beat of the mammalian heart is independent of the brain, whatever may be its dependence upon lower nervous centers.

Benjamin Collins Brodie was born at Winterslow in Wiltshire in the year 1783. His father was a clergyman of the established church. At the age of eighteen he went up to London to begin the study of medicine. In the early part of 1803 he came under the tutelage of the distinguished British physiologist, Sir Everard Home. It was to the influence of this scientist, undoubtedly, that we must attribute the turning of the young physician to scientific pursuits. It appears that his reputation as a physician and scientist rose rapidly, for seven years after his first connection with Sir Everard Home he was invited to deliver the Croonian lecture. This lecture is his first published contribution to physiology. He was elected a Fellow of the Royal Society the same year, and the next year, 1811, was awarded the Copley medal, being at this time twenty-eight years old. For certain surgical services performed upon the person of George IV. and his successor, William IV., he was knighted by the latter monarch soon after his accession to the throne of England. He died at his seat, Broome Park, Surrey, at the age of eighty.

Whether or no the work of Brodie was influenced by that of Legallois, the two British scientists who were the next to take up the study of the heart-beat were, according to their own statement, led to do so on account of the conclusion of the French scientist that the beat depends upon the spinal cord. In the year 1815 two papers were read before the Royal Society by Dr. Wilson Philip,[2] both of which dealt with the relation of the nervous system to the action of the heart. Philip showed, first, that the spinal cord of a rabbit could be totally destroyed, without affecting seriously the beat of the heart, provided artificial respiration were maintained. He also studied the effects of various stimulations of the cord on the heart. He found that the application of alcohol to the upper part of the cord, in frogs or rabbits, had the effect of quickening the beat, while watery solutions of opium or tobacco had the opposite effect. He observed that considerable pressure could be applied to the brain or cord without affecting the heart. His conclusions from his results were that the heart is independent of the central nervous system so far as normal activity is concerned, but at the same time is subject to its influence to a considerable degree.

Wilson Philip was for many years an active worker in the fields of physiology and pathology. He was born in Scotland about the year 1770. Of his parentage or birth-place nothing is known. His medical training was obtained in Edinburgh. He was a Fellow of the Royal College of Physicians both in Edinburgh and London, and also of the Royal Society of London. He was a successful practitioner, and accumulated a large fortune, but unwise investments swept it all away, and, in 1842, he was obliged to depart hurriedly from London to avoid being arrested for debt. He went to Boulogne and from there all trace of him is lost. His scientific work was considered of great importance in his day. He was one of the first to employ the microscope in the study of inflammation. His contemporaries speak of him with great regard because of his humane and rational methods of experimenting on living animals.

The other investigator whose interest was aroused by the work of Legallois was William Clift,[3] whose paper was also

[2] Philip, Proc. of the Royal Soc. London, 1815.
[3] Clift, *Ibid.*, 1815.

read before the Royal Society in 1815. This worker studied the effect of destroying the spinal cord in fishes. The particular species examined by him was the carp. He found that destruction of the cord by means of a fine red-hot rod had the effect of quickening the beat for three or four contractions, but after that was without influence on the heart. He pointed out that Legallois' result was due to the suddenness and violence of his operation. He made the incidental observation that the heart of the carp comes to rest when exposed to the water (presumably fresh) in which the fish is swimming, quicker than when exposed to air.

The life of this man, William Clift, is a very interesting one. He was born in a small town in Cornwall in 1775. His mother was left a widow while he was a small child, and his early years were spent in deep poverty. He was, however, able to attend school in the neighboring town of Bodmin. Here his taste for drawing came under the notice of Mrs. Gilbert, the wife of a local gentleman, and sister-in-law of the distinguished anatomist, John Hunter. This lady recommended Clift as an apprentice to Hunter on account of his quickness and his natural taste for drawing which, she said, was shown by his eagerness "to come into her kitchen in Cornwall, and make drawings with chalk on the floor." Arrangements for his apprenticeship to the anatomist were completed, and, in 1792, Clift came up to London to enter upon his service, his duties were to write at Hunter's dictation, to make drawings, to dissect, and to take part in the care of the museum which Hunter was establishing in the back part of his house. He was with Hunter only a year, when the connection was severed by the death of the latter. During this year the young apprentice conceived a strong affection for his master, and was always active in refuting the calumnies with which Hunter's envious rivals sought to detract from his reputation. Clift was employed for the next six years by Hunter's executors to care for the collections which his late master had spent years in accumulating. For this service he received the sum of seven shillings a week, and upon this amount he lived notwithstanding the fact that food was at war prices. During these six years Clift devoted himself to the care of the collections, with such success that when, at the end of this time, they were purchased by Parliament, they were in much better condition than at the death of Hunter.

In 1800, Parliament turned the collections over to the Corporation of Surgeons, a body which became afterward the Royal College of Surgeons. Clift was retained as conservator of the museum at one hundred pounds a year, and continued in this position for fifty years, retiring, ultimately, on his full salary of four hundred pounds a year. During his tenure of the curatorship he busied himself with researches in comparative anatomy and physiology, many of which were of considerable importance. He was a man of most lovable disposition, and was held in the greatest esteem by his scientific contemporaries. Through the influence of Sir Humphry Davy he was elected a Fellow of the Royal Society in 1823. Cuvier, Sir Charles Lyell, Sir Benjamin Brodie, and other scientific men acknowledge their indebtedness to him for information and help in completing their researches. He died in London in the year 1849.

After the appearance of these three papers which have been just spoken of, no further contributions on this subject were made to the Royal Society for thirty years, and with the exception of an isolated observation occasionally, no more work seems to have been done on the heart-beat in England for that length of time. About the year 1836, Todd's Encyclopedia of Anatomy and Physiology was published in England. This work was an attempt to give a complete résumé of the anatomical and physiological knowledge of that time. The chapter on the heart was contributed by John Reid, an anatomist of Edinburgh. In common with the other anatomists of his day, Reid delivered lectures and performed researches in physiology as well as in his own more particular subject. He begins the part of his article that is devoted to the causation of the heart-beat, by a review of the teaching of Haller on the subject. It will be remembered that Haller believed the irritability of the heart to be an intrinsic property of the muscle substance, and that this property is normally called into action by the stimulating influence of the blood upon the tissue. With regard to the question as to whether or not the heart requires the influence of the blood or any other stimulus to call it into action, Reid quotes an experiment,[4] apparently his own, in which the heart of a frog was placed under the receiver of an air-pump and the air exhausted from around it. The beat continued undisturbed under these conditions, although the possible stimulating action of the air was excluded. He does not accept this, however, as conclusive evidence that the heart is able to beat without direct stimulation, because, as he says, the mere contact of the organ with the surface upon which it is lying may be sufficient stimulus for a structure having such excessive irritability as the heart may be supposed to possess. In connection with his discussion of the influence of the blood on the heart-beat, a curious notion crops out, which seems to have been quite prevalent about that time. I have come upon the same notion in the writings of others of that period. The idea seems to have been that the chief function of the heart was to pump itself free of the blood that continually flowed into it. I quote Reid's own words on the subject. "When the blood is forced on more rapidly toward the heart, as in exercise, its contractions become proportionally more frequent. If the contractions of the heart were not dependent upon the blood, and their number regulated by the quantity flowing into its cavities very serious and inevitably fatal disturbances in the circulation would soon take place." Having concluded that heart muscle, like skeletal muscle, is directly dependent for every contraction upon some form of external stimulation, he passes to the question as to where the irritability of the heart resides. Is it a property of the muscle substance, or is it mediated only through the nerves of the organ? He quotes the experiments of Wilson Philip, Clift, and others which show that the heart is independent, at any rate, of the brain or cord. As will be brought out presently, those who still maintained the neurogenic origin of the heart-beat attributed it to sympathetic nerve centers outside the cord. Brachet,[5] a French observer whose work appeared in 1834 believed that it resided in the cardiac plexus, because he found that extirpation of this structure resulted in the immediate and permanent arrest of the heart. Reid

[4] Reid, Todd's Encyclo., Vol. II, p. 611, 1836-39.

[5] Brachet, Rech. exp. sur les fonct. du syst. nerv. ganglion. Paris, 1830, p. 163.

questions the conclusiveness of Brachet's experiment on the ground that so much time was required for the operation, and so much injury to heart tissue was involved in it, that it would be a matter of surprise to find the heart beating at its end. While he admits that there is abundant evidence for the fact that the heart is influenced to a greater or less extent by the central nervous system, Reid nevertheless concludes that the sum-total of knowledge indicates that the heart muscle possesses in itself the property of responding to stimulation by contraction.

The facts that I have thus far recorded, show clearly, I think, that among English physiologists there was very little inclination to depart from the views originally expressed by Haller, so far, at least, as they looked upon the irritability of the heart as a property of its muscular substance. What little insight we have had into the French standpoint has indicated that among the workers of this land the neurogenic theory was looked upon with favor, to say the least. I wish now to give some account of the views which were being developed in Germany during this same time. I am indebted to the article in Wagner's Handwörterbuch der Physiologie, Vol. II, by G. Kuerschner,[6] on this subject, for most of the facts which I am able to present concerning the German point of view, up to his time, 1844. Unfortunately I am unable to give any account of this man's life, nor to form any estimate of his fitness for the task of presenting the theories of his time regarding the topic in hand. The fact that he was selected to discuss the subject of the heart's activity in so important a work as Wagner's Handwörterbuch would seem to be sufficient guaranty of his fitness for the task, but the curious theory he proposes in explanation of the heart-beat would lead one to doubt his possession of conservative judgment. No one is mentioned in the Cyclopedie der Aertzte, nor in the large German national encyclopedia of biography with whom I could certainly identify him. His references are by no means so complete as might be desired, hence I shall be obliged to refer to much of the work done in Germany in general terms.

The German method of attacking the problem, according to Kuerschner, was to make careful comparative studies of the heart, both with skeletal and plain muscle, and then draw conclusions by reasoning from analogy. The histological and chemical studies of the heart that were made during the early years of the nineteenth century, indicated a close resemblance between the structure of the heart and of skeletal muscle. The question as to whether the heart muscle could be made to respond to stimulation in the way in which skeletal muscle does, was for a long time the subject of much controversy. The discussion included both the question as to whether or not the heart could be directly stimulated, and the problem of its responsiveness to stimulation through its nerves. Volta, Valli, Klein, Pfaff, Behrends, and Bichat decided that direct galvanic stimulation of the heart's substance was without effect upon it so far as arousing activity was concerned. Humboldt,[7] Fowler,[8] and Nysten, on the other hand, were able to prove conclusively that under proper conditions the heart could be excited to definite motor response by galvanic stimulation. The Italian physiologist, Fontana, observed that in spite of strong mechanical stimulation, such as pricking with a sharp instrument, the diastole of the heart proceeded to its end. He interpreted this to mean that the heart does not respond to this sort of stimulus. Other observers, however, were able to show that if the mechanical stimulus is properly applied, response can be obtained also to this kind of stimulation. Equally discordant results were obtained in the attempt to determine whether the heart can be stimulated through its nerves. Humboldt reported that he was able to excite a heart to contract by galvanic stimulation of the nervi cardiaci. Burdach [9] found that either chemical or mechanical stimulation of the cervical sympathetic in dying rabbits, strengthened the contractions of the heart. Neither Kuerschner nor Joh. Mueller could obtain the result reported by Burdach, although Kuerschner reports a single instance in which each stimulation of the common vago-sympathetic trunk in a dying dog was followed by a single contraction. Valentin [10] and Volkmann observed variations in the heart-beat after stimulation of the spinal accessory nerve within the cranial cavity. In spite of these variant results the conviction fastened itself upon the minds of practically all the workers in this field, that the heart, like skeletal muscle, can be stimulated either directly or through its nerves. The great similarity of the heart to skeletal muscle in so far as ordinary response to stimulation is concerned, having become generally admitted, the next problem to be faced was the comparison of the rhythmicity of the heart with that of structures in which ordinary skeletal muscles are involved. To those who were looking for analogies between the action of the heart and that of organs whose activity is admittedly of nervous origin, this study very soon developed facts which seemed to offer conclusive proof of the neurogenic origin of the heart's activity. The most important of these was the observation that as a heart is gradually dying, its rhythmic property disappears before the power of the individual fibers to respond to stimulation is lost. It was also shown by Kuerschner that if a heart be cooled down with ice-water, any of its chambers can be provoked to response by proper stimulation without the contraction spreading so as to involve other chambers than the one stimulated. Strictly analogous phenomena in other rhythmic structures, structures whose activity is evidently nervous, are quoted by Kuerschner. He says, for instance, that if the brain of an animal be destroyed, the contractions of the œsophageal muscles in swallowing are orderly and normal at first, but subsequently this sequence disappears and then stimulation of any muscle is followed only by contraction of that muscle, and not by the entire act of swallowing as at

[6] Kuerschner, Wagner's Handwörterbuch d. Physiol., 1844, Vol. II, p. 70 et seq.

[7] Humboldt, Gereizte muskel- und nervenf., Vol. I, p. 312, 1797.

[8] Fowler, Exper. on Animal Electricity. London, 1794.

[9] Burdach, Physiol., Vol. IV, p. 464.

[10] Valentin, De funct. nervorum cerebral et symp. Berne, 1839.

first. He cites as another example of the same sort, that if the head of a lizard be severed from its body just behind the occipital foramen, the respiratory movements of the head and neck continue normal for a time, but ultimately local stimulation meets only local response, as in the case previously cited. I shall give you Kuerschner's reasoning from these facts in his own words:

"These experiments teach that, in general, rhythmic activity is dependent upon the central nervous system, and not upon the muscles. It is well known that the central nervous system loses its irritability as the result of decapitation or poisoning much quicker than do the muscles. In this the heart is analogous. It loses its rhythmic property before the power of the individual muscles to respond to stimulation is lost. The conclusion can scarcely be avoided that in the heart the combination of contractions of the different parts results, not from the irritability of their muscle masses, but from the combination of these muscle masses, by means of nerves, with a central organ of the nervous system. Hence all hypotheses for the explanation of the heart's rhythm which go back to the independent irritability of the heart tissue are excluded. Among them must be placed the opinions of Haller."

The argument, which I have just given appeared to the German physiologists perfectly sound and conclusive. The question as to what central nervous organ is to be looked upon as the source of the heart's rhythmic action promised, however, to present some difficulty. The experiments of Brodie, Philip, Clift, and others had showed beyond doubt that neither the brain nor the spinal cord is essential to the rhythm of the heart. Magendie had removed all the sympathetic ganglia of the neck, along with the first dorsal ganglion, without disturbing the heart's action. There was also to be considered the fact of the long-continued beat of the isolated cold-blooded heart. To meet all these difficulties, Joh. Mueller advanced the idea of intra-cardiac ganglia. Fortunately for his suggestion, the existence of ganglion cells in the heart was shortly demonstrated by Remak,[11] Volkmann, Bidder, and by Mueller himself. To add to the assurance which this discovery gave, it was shown that these nerve cells are most abundant in those parts of the heart in which its rhythm originates, and in which experiment shows it to be most irritable, namely, the venous portion. Investigators were unable to prove experimentally that the rhythm of the heart depends upon the intra-cardiac ganglion cells, but they made a great deal of a clinical case reported by Dr. J. Heine,[12] son of the distinguished orthopedic surgeon of that name, from one of the Vienna hospitals, in the year 1841. The case was of a man whose *"nervus cardiacus magnus"* was bound up into a black knot the size of a hazel-nut just beneath the arch of the aorta. The nerve was somewhat thickened where it entered into the knot. This man suffered from periodical intermittence of the heart-beat. The interpretation of this case was as follows: The heart must be under the influence of the nervous system, or this malformation of the cardiac nerve would have had no effect. On the other hand, the seat of the heart's dependence must be lower down than the level of this disturbance or, instead of presenting the phenomenon of periodical intermittence, the heart would have stopped beating altogether.

A satisfactory nervous mechanism for carrying on the heart-beat had now been supplied. It remained to suggest, and if possible prove, the way in which this mechanism acts to bring about the rhythmic beat of the heart. Joh. Mueller[13] proposed an ingenious hypothesis which involved a conception of the mode of action of the sympathetic ganglion cells that has persisted in physiology to a greater or less degree even up to the present. He was led to his idea by the observation that when the cœliac ganglion is stimulated with potassium hydrate or some similar agent, in a rabbit with exposed viscera, there is a long latent period between the application of the stimulus and the response of the intestines.[14] He concluded that the sympathetic ganglion cells bear the same relation to the nerve impulse that the leyden jar does to the electric spark. In other words, the ganglion cell requires to be charged, an operation which consumes a certain amount of time. Based upon this assumption, Mueller's explanation of the rhythmic action of the heart was as follows: A steady stream of impulses is to be conceived as flowing into the heart from the central nervous system. These impulses, instead of arousing the heart, accumulate in the ganglion cells until they reach a certain maximum, when they are discharged all at once, producing their effect upon the heart. By assuming this property for the cells of the sympathetic ganglia, the rhythmic nature of the heart-beat is satisfactorily explained. Kuerschner takes exception to Mueller's hypothesis on two grounds, in the first place he says that the assumption of a peculiar property for the sympathetic cells, different from that possessed by precisely similar cells in the cord, is entirely unwarranted. Moreover, he argues, the beat of the heart like the action of every other bodily organ, should be looked on as purposeful, adjusting itself to the varying requirements of its function. According to the hypothesis of Mueller, the action of the heart is regulated entirely from the outside, and no mechanism is suggested by which the necessary adaptations can be made. In all the other rhythmic structures of the body, the respiratory apparatus, the œsophagus, the intestines, etc., a means of suiting the activity of the structure to the work it has to do exists. Why then may we not look for a similar regulatory device in the heart?

In proposing a hypothesis on his own account, Kuerschner sets out to fulfil the following conditions. He must provide a way by which rhythmic nervous stimuli can fall into the heart from the ganglion cells imbedded in its own substance. These rhythmic nerve impulses must be adapted so that they can vary with the varying needs of the body, and they must also be under the influence of the external stimuli which are

[11] Remak, Mueller's Archiv, 1844, p. 463.
[12] Heine, Mueller's Archiv, 1841, p. 234.
[13] Joh. Mueller, Physiologie, 1843, Vol. I, p. 630 et seq.
[14] Joh. Mueller, Physiologie, Vol. I, p. 631.

continually falling upon the heart from the blood flowing through it. He lays great stress upon the idea that the most satisfactory way in which a purposeful adjustment of the heart's action can be imagined, is by the supposition that every response of the organ comes as the result of a definite stimulus which reaches it from the outside, usually through the blood. All experiments indicate that the heart beats only in response to stimuli. In the cases in which excised hearts continue active for a long time, the air can be looked upon as the efficient stimulus. Even the experiment of Reid, in which a heart continued to beat in an exhausted chamber, is an illustration of the same principle, for when one considers the great pressure of the ordinary atmosphere, he could not expect otherwise than that the withdrawal of so great a load should act as a most efficient stimulus. It is evident that the simplest, if not the only way, by which stimuli applied to the surface of the heart can bring about the discharge of nerve cells, is through a reflex mechanism. Kuerschner proposes, then, to see if a reflex arc can be logically established within the heart, and if so, to inquire whether a rhythmic source of sensory stimulation can be demonstrated. "No one can doubt," says Kuerschner, "the existence of sensory nerves in the heart. The pains which arise in diseases of that organ are proof enough." He finds also another proof of their presence in the fact noted by Haller, that the inner surface of the heart is more sensitive than the outer one. Moreover, Henry[15] and afterwards Joh. Mueller,[16] found that opium and nux vomica were without effect on the outer surface of the heart, but promptly arrested its beat when applied to the inner surface. The conclusions to be drawn from these results are: 1st, that the action of the stimulus in the one case, and of the drug in the other, was upon sensory nerves; 2d, that these nerves are more abundant on the inner than on the outer surface of the heart. It is scarcely to be supposed that if the action were simply upon muscle substance one surface would be found to differ in response from the other one. If it be admitted that sensory nerves are present in the heart, some normal function for them is to be sought, for it is scarcely to be supposed that sensory nerves are present for no other purpose than to give warning of disease. The simplest explanation of their function that can be offered is to suppose that they form the sensory side of a reflex mechanism. The fact that the response of the heart to stimulation is always orderly, no matter to what part of its surface the stimulation is applied, is another argument for the idea that stimulation affects sensory nerves. The stimulus may be applied at the tip of the ventricle, but if the heart is in good condition the response always begins at the auricle and sweeps over the heart in the usual way. Only two other explanations for this fact are possible. Unless the stimulus at the tip of the ventricle affects a sensory nerve, the impulse must be transmitted through the muscle substance itself to the auricle, or else motor nerves on their way to the venous part of the heart must curve around so as to pass by the tip of the ventricle. Moreover, since stimulation at any point on its surface results the same as at the tip of the ventricle, it would have to be supposed that motor nerves lead from every part of the heart to the auricle. By far the most sensible view, in Kuerschner's opinion, is to admit the presence of sensory nerves. Having demonstrated to his own satisfaction a reflex arc, Kuerschner now proceeds to seek for a normal rhythmic source of sensory stimulation, by which his reflex mechanism may be operated. It is evident at once, that this source of stimulation is to be found in the blood. Not only must this be the case in order that the heart may fulfil its function as a purposeful mechanism, but no other possible source of stimulation presents itself. There are two alternatives as to the way in which the stimulating action of the blood may be exerted. It may stimulate chemically or mechanically. Four considerations are presented by which, according to Kuerschner, chemical stimulation is excluded: 1st, if the stimulus of the blood were chemical, a single drop should be as effective in arousing a response as a large quantity, hence the heart, under these conditions, would never have a chance to become filled with blood, but as soon as the first drops entered it the next contraction would ensue; 2d, it is a general law of the body that wherever chemical stimuli are in play, not serous but mucous membranes are present, whereas in the heart, as is well known, serous membranes are the only ones that exist; 3d, a fluid which feeds the heart, cannot well act at the same time as a chemical stimulus to it; 4th, if the stimulus is chemical, the two sides of the heart must have entirely different sorts of irritability since they react alike, while one side contains only arterial blood, and the other only venous blood, a fluid differing from arterial blood so far as its chemical nature is concerned, to a very marked degree. This last great difficulty in explaining the similar action of the two sides of the heart, is entirely obviated by the assumption that the stimulating action of the blood is mechanical, for arterial and venous blood are perfectly similar so far as physical characteristics are concerned, and so would have, as a matter of course, equivalent mechanical effects. Another, and quite distinct, set of phenomena also argue strongly in favor of the view that the influence of the blood upon the heart is mechanical. These are the phenomena connected with the rise of cardiac sensations into consciousness. Such sensations appear to us always as pressures. The pains which result from diseases of the organ are pains of too severe pressure. The heart sensations which we have as the result of violent emotions are sensations of pressure. Trouble, grief, and care press upon the heart. Observations show that often acute inflammations of the heart substance are felt only as pressure in the heart region. Kuerschner now proceeds to show how the mechanical stimulus works and begins by enunciating what is to him the vital point of the whole proposition. This point is as follows: "It is not to be assumed simply that the stimulus for contraction is aroused when the heart is full of blood, but *when it can be filled no further.* The contraction is thus aroused at the instant most suited to the needs of the circulation." When he begins to develop this

[15] Henry, Edinburgh Med. and Surg. Jour., 1832.
[16] Joh. Mueller, Physiologie, Bd. I, p. 636, 1840.

idea, which he does by attempting to apply it to conditions under which the heart-rate varies, he involves himself at once in a maze of difficult and complicated argument. I will not weary you further with the pointless, and well-nigh endless mass of logic with which he attempts to establish his proposition. I wish to say, however, that in his argument the same idea appears as in the discussion of the same topic by John Reid, and of which I spoke in that connection. I refer to the idea that the purpose of the heart-beat is chiefly to unload the heart from the weight of blood which is constantly flowing into it. This theory of Kuerschner's was published in 1844. It seems to have attracted almost no attention, a fact which is to be explained, in all probability, by the circumstance that at about this time began a great flood of discoveries which, although not overthrowing the neurogenic theory, put an entirely new face on the whole problem.

In 1845 the brothers Eduard and Ernst Heinrich Weber discovered the inhibitory character of the vagus nerve, in its action upon the heart. This discovery ranks, undoubtedly, among the most important physiological contributions of the nineteenth century. In view of its great significance, a quotation from the authors' own account of their experiments may be of interest. Their paper appeared in the third volume of Wagner's Handwörterbuch,[17] the second part. I have found it convenient to paraphrase and abridge considerably their description. They report six series of experiments. In the first set they beheaded a frog and then stimulated the cord, having one electrode at the upper end and one at the lower. This procedure had no effect upon the action of the heart; nor did they obtain any when both electrodes were placed upon the cut upper end of the cord. When, however, in an unbeheaded frog they placed one electrode in a nostril and the other on the cut surface of the cord at the level of the fourth or fifth vertebra, stimulation was followed, after one or two pulsations, by complete standstill of the heart. When the stimulus was removed, the heart began, after a few seconds, to beat again; slowly and feebly at first, but after a short interval with the original rate and force. The standstill was in diastole, and the heart remained full of blood.

The second set of experiments were for the purpose of determining from what part of the nervous system this inhibitory influence proceeded. The head of a frog was separated from the vertebral column in such a manner that the heart, the lungs, and the abdominal viscera retained their normal connections with the head. The electrodes were placed close together on the cut upper surface of the medulla. Stimulation was followed by stand-still of the heart, sometimes completely, sometimes only partially, according as the animal was fresh and vigorous or not, according to the degree of exhaustion of the nervous parts, and according to whether the stimulating current were employed to advantage or not. The heart remained at rest under continued stimulation until the vagus nerve became fatigued, when, in spite of the stimulus, the heart resumed its normal activity. These effects arose entirely from stimulation of the brain, inasmuch as removal of the spinal cord did not, as we have just seen, produce any change in them.

To make a more exact determination as to what part of the brain these effects came from, the electrodes were placed very close together, and the brain of a frog, from which the roof of the skull had been entirely removed, was carefully explored. It was found that stimulation of the cerebral hemispheres has no effect upon the heart. When the corpora quadrigemina were stimulated, the heart came to rest after three contractions. To prove whether this result arose from the corpora quadrigemina themselves, or was due to spread of current to the medulla, a cut was made with great care between these two portions of the brain, leaving them, however, in contact. Stimulation of the corpora after this operation had not the slightest effect upon the heart. This experiment made it evident that this power to arrest the heart is present in the corpora quadrigemina. In order to determine the lower limit in the brain of this inhibitory function, a series of exploratory stimulations were made, beginning at the brachial plexus, and working up the cord. No heart effects were obtained from these stimuli until the level of the lower end of the calamus scriptorius was reached in the medulla. At this point stimulation caused standstill. The medulla was then sectioned at this point, and stimuli were applied first to the upper cut surface, and then to the lower. Stimulation of the upper surface caused standstill, but no effect was seen when the lower surface was tested. By this means they mapped out the area of the brain from which inhibitory fibers arise as extending from the corpora quadrigemina to the lower end of the calamus scriptorius in the medulla.

The next question was through what nerves the inhibitory influences are conveyed. One vagus in a frog was cut and stimulated peripherally without effect on the heart, but when both vagi were cut, and both stimulated at the same instant, the arrest ensued. Their conclusion was that this property of inhibition requires the combined influence of both these nerves for its successful accomplishment.

The sympathetics were studied to see whether they shared the function of the vagi in this regard. It was shown that they do not convey inhibitory impulses to the heart.

To ensure that the vagus effects were not due to escape of stimulus to the heart over these nerves, a device was prepared by which any current that might pass down either vagus, would be short circuited before it reached the heart. The effect of stimulation after this device was used was exactly the same as before.

This experiment completed the chain of evidence, so far as the frog's heart is concerned. It only remained to see whether the same mechanism exists in the warm-blooded animals. The Webers tried this upon a kitten four weeks old by exposing and stimulating the vagi in the neck. They found that the heart was arrested in the kitten, just as in the frog, and also that it would break through long-continued stimulation in precisely the same way.

[17] Weber, Ed., Wagner's Handwörterb. d. Physiol., Vol. III$_2$, 1846, p. 43 et seq.

The Weber brothers were led by their experiments, to draw the following conclusions as to the source of the rhythmic action of the heart. The sympathetic nerves were to be considered as the motor nerves of the heart. These act by innervating the intra-cardiac ganglia. These ganglia, however, must possess the power of independent rhythmicity to a large degree, since the isolated heart is able to beat. The vagus fibers are inhibitory, and their inhibitory power is exercised in the heart in exactly the same way as in other structures that are under nervous control. That is to say, they act by inhibiting the ganglia from which the normal impulses of the heart arise. When we recall the fact that the idea of the inhibition of nerve centers by means of nerve impulses was a familiar one at that day, whereas such a thing as direct inhibition of muscles through nerves had never been thought of, the conclusion of the Webers is seen to be the most natural one they could have drawn.

In 1850 Schiff[18] discovered the existence of the refractory period. His discovery was corroborated, and a careful study of the phenomenon made, by Kronecker and by Marey the following year. This discovery was helpful to those engaged in the attempt to explain the heart-beat, because it removed the necessity of providing a source of rhythmic stimulation. Since the heart is refractory during a part of its beat, all that is necessary in order to explain its rhythmic action is to demonstrate the existence of a source of constant stimulation. Its own property suffices to convert this constant stimulus into rhythmic response. To the "motor ganglia" in the heart substance was assigned this role, and this idea was regularly incorporated into the neurogenic theory.

In the early fifties the celebrated experiments of Stannius[19] were performed. This observer placed a ligature exactly at the junction of the sinus with the auricle and the part of the heart beyond the ligature stopped beating. He then tied a second ligature in the auriculo-ventricular groove and the beat of the ventricle was resumed. The explanation of the stoppage which followed the first ligation, was simply that the source of the nervous discharges upon which the heart depended for its action, Remak's ganglion in the sinus, had been cut off. To explain the revival of activity in the ventricle as the result of placing a ligature in the auriculo-ventricular groove, recourse was had to the fact that Bidder's large ganglion lies in this groove in such a position that ligation might stimulate it. To this ganglion was assigned a subsidiary emergency role. Although supposed to be normally inactive so far as influencing the heart's rhythmic beat was concerned, it was supposed, under this special stimulus, to become active and efficient as a means of arousing the ventricle to contract rhythmically.

At the conclusion of the statement of the early work in England, mention was made of the fact that among British physiologists the myogenic theory of the heart's action remained generally in favor. Beginning about this time, 1850, a great many facts began to be brought out which strengthened the British position very much, and, as a matter of fact, put the believers in the neurogenic theory rather on the defensive. The experiments of Bernstein,[20] published in 1876, were especially welcome to them, because they formed the first important contribution to the neurogenic side of the argument during the period of twenty years succeeding the work of Stannius, a period which had been very productive of evidence on the other side. Bernstein showed that if a clamp were adjusted across the middle of a beating ventricle and then screwed tight, the portion of the ventricle beyond the clamp would come to rest. This portion of the heart had been shown to be free from ganglion cells, hence this experiment was interpreted as showing that parts of the heart which do not contain ganglion cells cannot beat if their connection with those parts in which nerve cells are present is cut off.

As recently as 1894 a strong argument in favor of the "motor ganglion" theory was advanced by Kaiser.[21] He based his argument upon a modification of the experiment of Stannius. It will be recalled that when a ligature was tied in the auriculo-ventricular groove of a heart which had been brought to rest by tying off the sinus, contractions were aroused again in the ventricle. Kaiser showed that if Bidder's ganglia were removed, ligation of the auriculo-ventricular ring was not followed by rhythmic contractions of the ventricle. He showed, moreover, that stimulation of the intact auriculo-ventricular ring is always followed by a series of several contractions, whereas stimulation of the same area after extirpation of Bidder's ganglia is followed by only one contraction for each stimulus, as is the rule for the heart-substance in general. The strongest opponents of the neurogenic theory were obliged to admit that Kaiser's argument, as based upon the experiments just quoted, was well-nigh incontestible, since no other reasonable explanation of his results can be given than to suppose that Bidder's ganglion has a motor influence on the heart's activity. An account of the way in which Kaiser's experiments were reconciled to the myogenic theory by its upholders, will be given in its proper place in connection with the review of the modern development of that theory. The present status of the neurogenic theory is practically that of Kaiser, since he is probably the latest to argue in its favor.

[18] Schiff, Arch. f. Physiol. Heilkunde, 1850, Vol. IX.

[19] Stannius, Arch. f. Anat., Physiol., u. wiss. Med., 1852, S. 81 et seq.

[20] Bernstein, Centralbl. f. d. med. Wissen., Berlin, 1876, S. 385.

[21] Kaiser, Zeitschr. f. Biol., München, 1894, Bd. XXX, S. 302.

THE JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read, and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly.

Volume XV is now completed. The subscription price is $2.00 per year. The set of fifteen volumes will be sold for $75.00.

THE PARTIAL OCCLUSION OF BLOOD-VESSELS, ESPECIALLY OF THE ABDOMINAL AORTA.

A PRELIMINARY REPORT BY DR. HALSTED.

At the meeting of the Johns Hopkins Hospital Medical Society, on March 20, 1905, a brief preliminary report was made of the results of a large number of experiments performed in the past year by Dr. Sowers and myself upon the abdominal aorta and other large blood-vessels of dogs.

It had occurred to one of us that possibly the aorta might be successfully occluded in man if the operations were undertaken in several acts instead of one. The notion of gradual compression in the ordinary use of the term was entertained only to be definitely discarded because of the seemingly insurmountable difficulty of preserving asepsis. A sinus must form about any instrument leading from the aorta to the air, and, sooner or later, such a sinus necessarily becomes infected. The method, therefore, should, we thought, be one permitting, in each entre-act, complete closure of the wound; the apparatus or material applied to the aorta should not be bulky nor endanger, by its form or substance, the adjacent parts; and it should admit of easy readjustment at subsequent operations. Metal bands of silver and aluminum were employed with the belief that at each operation the amount of constriction could be regulated to a nicety. With the aid of a clever jeweller an instrument was devised to curl the metal strip, in situ, in perfect cylinder-form, about the vessel. The tightening of the band, the cylindrical form being preserved with great care, was completed with fingers and tweezers, but ultimately, when narrower bands were used, the tweezers could, fortunately, be discarded. The instrument for curling the band was also in the majority of cases finally dispensed with.

We attempted rather persistently but unsuccessfully to determine accurately the blood pressure in the femoral arteries during and after the application of the band; and Dr. Haller is now devising and constructing for us an instrument on the principle of the Erlanger instrument to enable one to determine the blood pressure in small and large arteries without dividing them. Calculations, therefore, as to the amount of occlusion were roughly determined by the fingers on the aorta and femorals.

For some weeks we feared that the sharp edges of the bands would cut through the pulsating and constricted aorta, and considered several methods to obviate, if necessary, this danger. On the twelfth day of the operation a dog died from hemorrhage, the result of ulceration at the upper edge of the band and we feared that the procedure might be doomed; but no further hemorrhage occurring we resumed, in a few weeks, the experiments. Then, after about 3 months, investigating in several dogs the conditions at the site of the band, we found to our chagrin, that just as we had feared, the wall of the aorta embraced by the band was, in almost every instance, atrophied, being reduced in some cases to hardly more than a film in thickness. Notwithstanding this observation the experiments went on uninterruptedly, a new series being instituted with the hope that, with an improved technique, and the employment of narrower and thinner bands, the walls of the arteries might retain their vitality, at least for a time sufficiently long to justify a second interference, and possibly the complete interruption of the blood current at a point just above the band. The width of the bands was reduced from 4 or 5 mm. to 2 or 3 mm., and the thickness from 32 and 33 degrees of fineness to beyond the highest numbers of our sheet metal scale, to what we term Nos. 37, 38, 39, and 40. On the carotids and femorals metal still thinner might perhaps be used. Bands so narrow and so very thin are easily rolled with the fingers. It is well to give the band approximately the proper curl before placing it on the artery. From the very first experiment we endeavored in each instance to roll the band as perfectly, as cylindrically, as possible, flattening of it being studiously guarded against for obvious reasons. Attempts to diminish the blood pressure very gradually and with accuracy are, of course, made futile by an imperfection in the rolling of the band. A flattening or imperfectly rolled band might, even if loosely applied, injure the intima and so cause thrombosis and completely interrupt the circulation. For these and other reasons silver wire, which was tried, was found impracticable. About ninety experiments were made on sixty-eight dogs. The technique of our operating rooms at the Johns Hopkins Hospital was observed in every particular and hence much time was consumed by the operations; but we are well repaid for the care exercised by the absence of wound infection. The buried, continuous, silver wire suture of the skin and rubber gloves for operator and assistants seem invaluable in experimental surgery when wound infection must be avoided. We are greatly indebted to Messrs. Cowles, Faris, Haller, Langford, and other fourth year students for their faithful assistance and interest and useful suggestions.

Summary.

(1) Thrombosis has not been observed in a single case. In a few of the specimens, however, proximal to the band, in the occluded artery, a little caruncle-like body, suggesting the substitution of a minute clot, has been present.

(2) Applied tightly enough to completely interrupt the circulation, the band has caused atrophy and sometimes complete absorption of the aortic wall; in such cases hemorrhage has invariably been prevented by the formation of connective tissue.

(3) With two or three exceptions there has been no evidence of adhesion of the folded intima *under the band;* aortic walls folded on themselves so snugly that, the band being

still in place, water could not be forced through with a syringe, could easily be smoothed out and the full lumen reestablished on removal of the band.

(4) Less snugly, loosely, and very loosely applied bands may remain on the aorta, femorals and carotids for months without causing macroscopic injury to the walls of the artery. In experiments of this variety the band after, say, one hundred days, shimmers brightly under a normal looking peritoneum, causing no visible reaction, and it may be as easily removed from the aortic wall as when originally applied. The probe point of a fine scissors passed into the lumen of the aorta and thus on through the band, dividing it and the aortic wall, reveals a perfectly normal looking intima and an aortic wall which, on gross section, evidences no change in texture and usually none in color.

We are encouraged to believe that there may be a place in surgery for the partially occluding band. Recently we have twice had occasion to use it on the human subject.

Case I. *To the left common carotid was applied an aluminum band which almost occluded it.*—Even in this case slight head symptoms persisted for several months making it seem likely that complete occlusion would have been followed by severe symptoms if not by death. We regretted that, in this case, the band was inadvertently rolled tighter than intended; it could, of course, have easily been removed and reapplied but our notions being rather vague as to the precise amount of constriction which we desired and being unable to determine accurately the blood pressure distal to the band we decided to let it remain and note the results.

Case II. *A woman asphyxiated to unconsciousness by an aneurism of the arch of the aorta.*—She was restored to consciousness and temporary relief afforded by a tube passed into the right bronchus. The skiograph seeming to indicate that the aneurism was chiefly on the left side of the sternum and the condition of the patient being so desperate I decided, having watched her for nearly half a day, that she would live only a few hours unless surgery could assist her. We exposed carefully and freely, without opening either pleural cavity, the heart, the arch of the aorta and the large vessels at the root of the neck hoping possibly to be able to encircle the aortic arch with a band of metal between the origins of the innominate and left carotid arteries; but the aneurism involved the entire arch and thus defeated our very earnest efforts to carry out the plan. The patient succumbed on the operating table before we had entirely despaired of being able to do something for her relief, and while we were still endeavoring to make a path for the band.

The smaller arteries, the ligation of which endangers merely the life of the limb may prove as suitable for partial occlusion as the aorta (abdominal and thoracic) which has never been successfully ligated in man. Meagre as our knowledge of this subject is I should probably feel it my duty to test the value of partial rather than resort to complete occlusion of the aorta, common cartoid, popliteal and other arteries whose ligation is attended with great danger to life or limb.

The partial occlusion of arteries discloses a suggestive and, I believe, a promising field for investigation in physiology and experimental pathology.

The history of the subject will be considered in a subsequent article. Of particular interest to us is the discovery that Luigi Porta, about 1846, attempted partial occlusion of arteries by means of strips of diachylon plaster applied in a way similar to that described by Brewer, who so ingeniously and cleverly closes wounds of arteries by strapping them with an absorbable plaster.

NOTES ON NEW BOOKS.

Lectures on Diseases of the Nervous System. Second Series. *Subjective Sensations of Light and Sound, Abiotrophy, and Other Lectures.* By Sir William R. Gowers, M. D., F. R. C. P., F. R. S., pp. 150. (*Philadelphia: P. Blakiston's Son & Co., 1904.*)

This neat but inexpensive volume contains a collection of ten lectures, all of which have been published separately before, some as long ago as ten years. Nevertheless, their appearance in book form is undoubtedly opportune, for those who are already acquainted with them will surely find time to read them again, and for those to whom they are still new not only profit but also much enjoyment can safely be promised. If it were necessary to condense this review into six lines we might well content ourselves with Dr. Gowers' own, perhaps too modest, words: "The facts I have given you are commonplace. Many of them may have been known to some of you, some of them may have been known to many of you; but one fact I am sure is true of all my hearers—for it is as true of myself as of anyone—the commonplace is, of all knowledge, that which we can least afford to despise or disregard." The first lecture on "Subjective Visual Sensations" has been re-written and several points of interest have been added. The second lecture deals with subjective sensations of sound, tinnitus aurium in its various manifestations being discussed. In the third and fourth lectures—which treat of abiotrophy or diseases due to defect of life—the various forms of atrophy are dealt with. In the essay on metallic poisoning—with lead and arsenic—the discussion of the lead-line and the various manifestations of arsenical pigmentation makes very interesting reading, but not less so the digression on the use of the term neurasthenia, which contains suggestions that every medical practitioner must ever keep in mind.

The other subjects dealt with are: Syphilis of the nervous system, inevitable failure, a study of syphilitic arterial disease, syringal hemorrhage, myasthenia and ophthalmoplegia and the use of drugs. That "the last, although given some years ago, seems to need no change in consequence of fresh knowledge" is undoubtedly true, but some amplification of the subject would certainly have been acceptable. The book is full of facts and of observations that are very helpful and suggestive, and should find a place in every medical library.

The Intestinal Catarrhs. Second edition. By Edward Blake, M. D., F. R. C. S. (*Chicago: W. T. Keener & Co., 90 Wabash Avenue, 1905.*)

This work has been published in response to a complaint from many sources that there is no English treatise on the intestinal catarrhs. It is apparently a clinical study of colitis, appendicitis, and their allies, with a section on sprue. The first chapters are concerned principally with the definition and the variety of names which are given to the condition which we usually term mucous colitis. The writer quotes seventy-six synonyms as applied to the

general catarrh of the intestinal tract. As, however, among the titles under which the author states that general catarrh of the intestines is "vaguely recognized" we find rickets, tabes mesenterica, Graves' disease, gout, rheumatic gout, dilated stomach, urticaria, psilosis, Cochin-China diarrhœa, not to speak of chordapsus, phantom tumor and senile enuresis, we must confess to being slightly puzzled.

Dr. Blake would assign the beginnings of colitis to a very early stage of existence. The occurrence of mucin and albumen during the first week of life is the first suggestion of the possibility of colitis. In an examination of the book we suddenly find a discussion of albuminuria in early life and then the report of a case of pyelitis from colitoxin. The special importance of this we rather fail to see, as also the report of a case of cystitis due to bacteriuria. Then follows a section on certain of the organisms found in the intestines. Again abruptly after this we are given a discussion of the causation of pancreatitis, cholecystitis and gall-stones. With this is an explanation of the secretion of the pancreatic juice. The startling statement is made that colitis is essentially an affection of the skin, by which the author apparently means that conditions in the skin are essentially associated with the colon. But in almost the next paragraph it is stated that gout apparently is the essential causative factor in colitis, and then a few lines further on that lack of ability to digest starch is the most important causative factor. A little later on we are suddenly thrown into a discussion as to the causes of infantile diarrhœa.

Then follows a discussion of the cause of colitis, which is described as being either of neural or inflammatory origin. In connection with this we are given the report of a patient who had colitis with "tobacco toxis" simulating abdominal aneurism. The most interesting point in his history seems to be that he was about to effect a separation from his wife on account of her bad temper. We then unexpectedly find a section on the influence of colitis on blood-pressure and the intestinal origin of arteriosclerosis, from which we learn that sclerosis and hypertrophied heart are often early results of colitis. This illuminating sentence must be noted: "Chronic intestinal catarrh gives rise to tachycardia in women until Graves' disease is replaced by myxœdema." After this it is pleasing to find some reference to two of our colleagues: "A much more valuable contribution to our knowledge of this most important subject, reaches us from the bank of the Chesapeake in far-off Maryland. No fewer than four thousand cases, many of them drawn from Osler's Clinic at the Johns Hopkins Hospital at Baltimore, have been 'boiled-down' by our indefatigable Transatlantic Brethren; and the resultant Extract of Pathological Pabulum, is of great suggestiveness: it is 'Meat,' indeed." In the opinion of Drs. Thayer and Brush, the "Chefs de Cuisine," the leading Etiological factors are:—

a. Physical Labour, sustained and violent.
b. Alcohol.

As to the acute diseases which predispose to Arteritis:

a. Rheumatic Fever takes the premier position.
b. Enteric Fever comes next, and
c. Malaria—stands third.

The author then points out that enteric fever—second on the list—is a "specialized form of colitis." To consider typhoid fever as a form of mucous colitis is a weird idea.

Then follow descriptions of gastric crises, dilated stomach, displaced kidney, floating kidney, hæmaturia, false floating kidney, orthostatic albuminuria from movable kidney, all of which, while undoubtedly interesting, hardly seem to be applicable in the present volume. Then come sections on elimination, infantilism, and the record of a case of "colitic infantism" in which, after an account of the patient's condition, we learn that he has done well at the university and has now to shave three times a week. Then follows a section on the physical characters of mucus and the description of some of the symptoms of mucous colitis, in which we find the note of a case in which the pain of pleurisy had been treated as a colic. This is no doubt an important observation but its bearing on the subject does not seem evident. The association of colitis with a number of diseases is referred to, but there is nothing of special moment brought out except that the author tends to lay great stress on its association with gout.

Next follows a chapter on "idiopathic colitis or dysentery." It is sad to learn from this that those of us who consider that amœbæ and certain organisms are etiological factors in dysentery are entirely wrong. There are many sections which it is absolutely impossible to review, among them being a discussion of typhus fever. The association of this with colitis we fail to see. Enough has been given to show the general character of the work. The latter part of the book is as much a jumble as the first. Altogether it is a most remarkable book. That it sheds any light on the subject of which it treats is doubtful. That it will furnish amusement to whoever takes the time to read it requires only the proof of a few minutes' perusal. We fear that the complaints from many sources which were the reason for the writing of the book will not be stilled by this response.

Report on the Origin and Spread of Typhoid Fever in the U. S. Military Camps during the Spanish War of 1898. By Walter Reed, Major and Surgeon, U. S. Army, Victor C. Vaughan, Major and Division Surgeon, U. S. Volunteers, and Edward O. Shakespeare, Major and Brigade Surgeon, U. S. Volunteers. Two volumes. (*Washington: Government Printing Office. 1904.*)

It would be remembered that an abstract of this report was published in 1900. We now have it in detail. Of the value of this work it is difficult to speak too highly. It is worthy to take a place with the Medical and Surgical History of the War of the Rebellion. The commission was composed of Major Shakespeare, Major Reed, and Dr. Vaughan of Ann Arbor. Unfortunately, the first two died before the report was completed, so that it had to be finished by Dr. Vaughan. In the letter of transmittal he pays a deserved tribute to the memory of his colleagues. From it we learn that Major Shakespeare worked especially on the question of the dissemination of typhoid fever, and the carefulness of the work in this report is a monument to his industry and zeal. To Major Reed fell especially all matters concerned with the application of sanitary measures.

The report is transmitted in two volumes, the first containing the detailed reports and the second the maps and charts. When one goes over the careful study of the sickness in each regiment and company one realizes what a tremendous amount of work has been done. The tables and summaries are very clearly gotten up and add greatly to the value of the work.

Many of the lessons to be learned from this report have been commented upon previously. As regards the spread of the disease the most important point established is the frequency of direct infection under such conditions as we have when large bodies of troops are collected together, and with this the importance of proper disinfection of the excretions as a preventive. Another fact brought out was the sad lack of ability to recognize typhoid fever in the surgeons who had charge of the troops. This was probably not so much their fault as that of the methods under which they had received instruction.

Some of the more important conclusions of the commission may be quoted:—

1. During the Spanish war of 1898 every regiment constituting the First, Second, Third, Fourth, Fifth, and Seventh Army Corps developed typhoid fever.

2. More than 90 per cent of the volunteer regiments developed typhoid fever within eight weeks after going into camp.

5. Typhoid fever became epidemic in camps located in the Northern as well as those located in the Southern States.

6. Typhoid fever is so widely distributed in this country that one or more cases are likely to appear in any regiment within eight weeks after assembly.

10. These investigations confirm the doctrine of the specific origin of typhoid fever.

11. With typhoid fever as widely disseminated as it is in this country, the chances are that if a regiment of 1300 men should be assembled in any section and kept in a camp the sanitary conditions of which were perfect, one or more cases of typhoid fever would develop.

13. Typhoid fever is more likely to become epidemic in camps than in civil life because of the greater difficulty of disposing of the excretions from the human body.

15. Camp pollution was the greatest sin committed by the troops in 1898.

20. Superior line officers cannot be held blameless for the unsanitary condition of the camps.

21. Greater authority should be given medical officers in questions relating to the hygiene of camps.

22. It may be stated in a general way that the number of cases of typhoid fever in the different camps varied with the methods of disposing of the excretions.

24. The regulation pit system is not a satisfactory method of disposing of fecal matter in permanent camps.

25. In permanent camps, where water carriage cannot be secured, all fecal matter should be disinfected and then carted away from the camp.

26. Infected water was not an important factor in the spread of typhoid fever in the national encampments in 1898.

28. Flies undoubtedly served as carriers of the infection.

29. It is more than likely that men transported infected material on their persons or in their clothing and thus disseminated the disease.

31. It is probable that the infection was disseminated to some extent through the air in the form of dust.

33. When a command badly infected with typhoid fever changes its location it carries the specific agent of the disease in the bodies of the men, in their clothing, bedding, and tentage.

41. Malaria was not a prevalent disease among the troops that remained in the United States.

42. The continued fever that prevailed among the soldiers in this country in 1898 was typhoid fever.

45. About one-fifth of the soldiers in the national encampments in the United States in 1898 developed typhoid fever.

46. Army surgeons correctly diagnosed about half the cases of typhoid fever.

47. The percentage of deaths among typhoid fever cases was 7.61.

Altogether we regard this as one of the most important studies of typhoid fever that has ever been made, and would recommend its careful study to all who are in any way concerned in dealing with the disease. That our knowledge of disease is so increased must be regarded as one of the advantages of the war. Neither the report of the sanitary work in the South African nor the Spanish-American War is pleasant reading for one who believes in the supremacy of the Anglo-Saxon race, but we may hope that the lessons have been laid to heart.

Operative Surgery. By Joseph D. Bryant, M. D., Professor of the Principles and Practice of Surgery, Operative and Clinical Surgery, University and Bellevue Hospital Medical College; Visiting Surgeon to Bellevue and St. Vincent's Hospitals, etc. Two volumes. Fourth edition. Entirely revised and largely re-written. (*New York and London: D. Appleton & Co., 1905.*)

Volume I treats of general principles, anæsthetics, antiseptics, control of hæmorrhage and shock; treatment of operation-wounds and ligatures of arteries; operations on veins, capillaries, nervous system, tendons, ligaments, fasciæ, muscles, bursæ, and bones; amputations and deformities; plastic surgery; operations on the mouth, pharynx, nose, œsophagus, and neck.

Volume II considers operations on the viscera connected with the peritoneum, the scrotum and penis, and miscellaneous operations, including those for some deformities of the external ear.

The first volume is excellent, and with very few exceptions, such as the omission of any mention of injection of the branches of the trifacial nerve with osmic acid for neuralgia, as described by Murphy of Chicago, or of Finney's method of building up the nose, where bones and cartilages have disappeared, by utilization of the phalanges of the left little finger, is up to date and complete.

The second volume covers the ground it undertakes in an equally satisfactory manner, and practically all of the newest operations are taken up and well described.

The illustrations, about 1800 in number and many of them colored, throughout are well chosen, and aid a great deal in explaining the operative methods. Instead of the usual lists of instruments required for different operations, there are photographs of the instruments themselves.

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The book is a valuable one, and will be of great use to practical surgeons, and also to practitioners and students who desire to familiarize themselves with modern surgical methods.

Transactions of the American Röntgen Ray Society. (*Philadelphia: A. H. Sickler Company, 1905.*)

This volume contains the transactions of the fifth meeting of the American X-ray Society, held at St. Louis.

The general tone of the articles is much superior to those appearing in the former transactions. There are a number of excellent articles in it, but the most important and interesting is the symposium on malignant disease and the discussions following. Practically every one holds the view that deep-seated and inoperable growths cannot be cured and at best but a temporary checking of the growth with relief of pain may be accomplished.

Carcinoma is purely a surgical disease and should not be given X-ray treatment unless the case is inoperable or the patient cannot undergo an operation. In superficial epitheliomata the results obtained from X-ray treatment are good but, as the symposium points out, we are restricting that class of cases more and more to those where the danger of metastases is not so great.

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CONTENTS.

PAGE

The Herter Lectures. Lecture I. The Contributions of Pharmacology to Physiology. By Hans Meyer, ... 351

Observations on Several Cases of Acute Pancreatitis. By William Sydney Thayer, M. D., ... 355

Diaphragmatic Grooves on the Liver. By Robert Orton Moody, M. D., ... 364

The Rise of the Present Conceptions as to the Cause of the Heart-Beat. II. The Myogenic Theory, and Modern Studies of Rhythmicity. By E. G. Martin, ... 377

PAGE

Proceedings of Societies:

The Johns Hopkins Hospital Medical Society, ... 384

Bilateral Exostoses on the Inferior Surface of the Calcaneus, Gonorrhœal in Origin (Pododynia Gonorrhoica); Perichondritis, Probably of Gonorrhœal Origin; Bronzed Diabetes, with Enlargement of the Liver and Palpable Spleen [Dr. Barker];—Inversion of Uterus [Dr. Williams];—Thoracic Aneurisms [Dr. Baetjer].

Notes on New Books, ... 387

THE HERTER LECTURES.

Lecture I. The Contributions of Pharmacology to Physiology.[1]

By Hans Meyer,

Professor of Pharmacology in the University of Vienna.

Ladies and Gentlemen:—Before I enter upon the task for which I ask your kind attention, I desire to express my hearty thanks for the great honor you have extended to me in inviting me to deliver the Herter Lectures. The honor I accept, not so much for myself as for the science which I represent.

Experimental pharmacology is a science with essentially theoretical aims—a part of general biology, in which there is nowhere shown a greater interest than in America. I take especial pleasure in asserting that in this land of varied successes the understanding of abstract problems and of purely theoretical work thrives and ever grows, always extending to wider circles, filled with a scientific idealism which invites the most splendid and admirable sacrifices, spiritual and material. Your famous university, and indeed these lectures themselves, owe their origin to such idealistic impulses. And this gives me the courage and the desire to talk to you of The Significance and Value of Pharmacology.

[1] Delivered at the Johns Hopkins Medical School, October 4, 1905.

It is, then, not necessary for me to claim your attention for the practical results or for their value to the practicing physician; not, however, that I undervalue this important side of pharmacology. But may I not hope at this place to be able to attain my purpose most easily, if I beg your attention to the biological results which we owe to pharmacological investigations?

For the explanation and analysis of physiological function, apart from comparative physiology, stimulation and extirpation of certain organs or parts of organs serve as general methods. Experimental physiology employed to this end mechanical and physical means almost exclusively. The scalpel and scissors, electrical, thermal, and mechanical stimuli have long served its purposes. The manifold means of chemistry have scarcely been utilized. Its appliances and its study belong, indeed, to pharmacology, which is, as an American fellow-worker has tersely said, "the experimental chemistry of protoplasm."

The drugs, that is, the chemical reagents, penetrate into the interior of the organs and reach parts which are not accessible

to the scalpel and the electric current. Indeed the differential action of poisons—that which has to do with single parts of organs or single especial groups of cells—is the important part of the pharmacological method. But, we must concede that it has not attained for the most part the undoubted certainty and clearness of physiological methods, for every drug which we wish to use as an instrument of investigation must first itself be investigated, its mode of action first be recognized and determined. And you all know well how difficult and equivocal such investigations are, and it is easily intelligible that, especially in the beginnings of such investigations, while there was no large array of pharmacological facts supporting one another, one scarcely ventured from these to draw far-reaching conclusions.

An interesting example of this sort is the admirable investigation of Felice Fontana on Indian arrow poison, which was carried out more than one hundred years ago. Fontana was forced to the conclusion, through ingenious experiments, which resembled the much later ones of Claude Bernard, that the arrow poison paralyzes neither muscle itself nor the whole nerve, but only the endings of the latter and that indeed the latter must possess a structure different from the nerves themselves, of which anatomy and physiology took no cognizance. Fontana, however, did not dare to draw the right conclusion because the proof was indeed a pharmacological and not an anatomical one. Only much later was it learned that properly conducted and correctly interpreted pharmacological experimentation possesses the same power of conviction as any other exact scientific method. And it is precisely the curara poison which has led to positive physiological discoveries. By its help Boehm and Nussbaum, through the discovery of the so-called paradoxical vagus action discovered the vasopressor nerves and the accelerator fibers in the trunk of the vagus nerve in dogs and cats; and later with the help of the same poison, Boehm obtained the proof, otherwise inaccessible to physiology, that the nerve endings in the muscles possess the same capacity for fatigue and recovery as the muscle itself. The important problem of the close connection between the irritability and the conductivity of nerves was not soluble except by the aid of the pharmacological method, that is, the methodical utilization of poisons like curara, veratrin, and carbon dioxide.

Formerly it was impossible to detect any physiological or morphological difference either in the arrangement or in the general structure of centrifugal and centripetal nerve tracts. But the narcosis experiments of Fraser, Alms, Joteyko, and especially the more recent ones by Dixon with cocain, showed that they must be chemically different from one another, inasmuch as they react differently to poisons.

Highly important, also, are the physiological results which Langley obtained with the help of nicotin poisoning in relation to the sympathetic ganglia. He was able to show that by means of nicotin the sympathetic ganglia, and through them all the pre-ganglionic nerves, were paralyzed, while the post-ganglionic nerves escaped. So it is possible to decide by this means whether a nerve ends in a sympathetic ganglion or passes through it, as is the case, for example, with the trigeminus fibers through the ciliary ganglion.

The study of the action of a wholly different type of poison, namely tetanus toxin, has also furnished a series of important facts relating to the field of neuro-physiology. If one injects into an extremity of a warm-blooded animal a sterile toxin derived from tetanus bacilli, there occurs, as is well known, a local tetanus, that is to say, the inoculated limb enters into tonic extension and shows especially in the later stages of the poisoning an increased reflex irritability, while all the remaining parts of the body continue to retain their normal position and normal reflex excitability. Now it was possible to show that this remarkable phenomenon arose through the circumstance that the poison was absorbed by the adjacent motor nerve-ends and carried upward in the axis cylinder to corresponding centers of the spinal cord. The blood and lymph channels are wholly unconcerned in this transportation of the poison, and there therefore remains only the possibility that there is constantly flowing through the axis cylinder of the motor nerves a centripetal protoplasmic stream, reaching as far as the ganglia of the neurones. This was a previously unknown fact which must be of significance for the nutrition of the nerves and also for the trophic disturbances of the central ganglia which develop after section of the peripheral nerves. This is also a point which is possibly of great practical importance. In a given case of infection with the bacilli of tetanus it is permissible to assume that a direct injection of tetanus antitoxin into the main nerve of the infected area, will serve to intercept and neutralize the toxin in its passage toward the central nervous system. I have also found that such a centripetal flow of diphtheria toxin occurs in the nerves and the same thing seems to be true of certain metals which like lead, give rise to chronic neuritic palsies. Perhaps a stream of this kind passes also along the sensory nerves, but in any case its course is arrested by the spinal ganglia, so that the tetanus poison is here held fast and is unable to reach the sensory apparatus of the spinal cord. If, on the other hand, one injects the posterior nerve-roots between the root ganglion and cord, there occurs an irritation of the sensory pain-exciting apparatus in the spinal cord, and indeed without simultaneous irritation of motor or reflex structures. There thus arises the pure so-called tetanus dolorosus which is characterized by the periodical recurrence of extremely painful seizures excited apparently through the summation of minimal and ordinarily wholly inactive stimuli. It makes no difference as regards the development of the phenomenon whether the spinal ganglion has or has not been removed,—a fact which was shown by Fletcher. In this manner has arisen the proof of the existence of wholly special pain-subserving structures in the central mechanism of the spinal cord (the existence of which was long denied by French physiologists)—structures distinct from those subserving tactile and motor functions.

Finally these investigations have brought to light another

remarkable fact. In the ordinary poisoning through tetanus toxin the muscles are the seat of two distinctly different kinds of phenomena. In the first place the involved muscles become shortened without undergoing contraction in the physiological sense. This condition may exist alone. In the resting state they show neither the electrical phenomena nor the heat production nor the muscle tone that characterize a state of activity. They shorten only slowly and the affected extremity thus becomes stiff and gradually immobilized. If the muscles have not undergone maximal shortening, they are still capable of voluntary or reflex contraction, as in the case of normal muscles. It is only later that we see the well-known strychnine-like reflex tetanus in which the muscles are implicated in rapidly recurring, increasingly accentuated contractions. Since it is possible to show that both the phenomena are subserved wholly by the spinal cord, it follows that there are present in the spinal cord various structures, quite distinct from the ordinary motor mechanism, which determine the state of inactive tension of the muscles, that is to say, their length while in a state of rest. These tonus-subserving structures are not excited by other poisons, like strychnine, and we have here the fundamental distinction between strychnine poisoning and poisoning by tetanus toxin. Indeed it was only by means of the latter poison that the existence of these length-regulating tonus centers in the spinal cord was brought to light.

I have spoken hitherto of the nervous system itself, but it is true that the physiology of structures closely connected with the nervous system, as the glands, heart, blood-vessels, and muscles has been materially advanced through the use made of pharmacological agents. You are all aware of the progress in our knowledge of lymph formation and the glandular function which we owe to studies of Heidenhain; and these again were dependent in a great degree upon the help of pharmacological methods involving the application of specific chemical stimuli. I shall mention the results of some more recent investigations in this same direction in the belief that they may be less familiar to you. Very recently Wertheimer and Lepage, in Lille, reported a series of pharmacological investigations on secretion by the pancreas which led them to important results. It has long been known that the pancreas may be stimulated to secretion in a reflex manner and also, as Pawlow showed, through direct irritation of the vagus nerve. We know also as a result of Starling's work that the pancreas can be thrown into activity directly through the specific chemical stimulus furnished by the presence of secretin in the circulating blood. Now Wertheimer and Lepage were able to show that the gland has at least two distinct mechanisms through which it is possible to excite the secretion of pancreatic fluids, first, certain structures intimately connected with the vagus nerve, which may be excited by pilocarpine, physostigmine or muscarine, or completely paralyzed by atropine; and secondly, another set of structures which are not acted upon by these poisons, being neither excited nor paralyzed by them, but which react to certain other definite chemical stimuli like secretin. Possibly the latter apparatus is part of the sympathetic nervous system; at all events the case of the submaxillary gland has been brought forward by Wertheimer and Lepage as analogous since in this case the terminations of the chorda may be influenced by pilocarpine and atropine, whereas the sympathetic nervous mechanism remains intact. And, finally, just as the salivary secretion differs according as it arises through the stimulation of the chorda or of the sympathetic nervous system, so does the pancreatic secretion resulting from the pilocarpine differ from that which is obtained through the action of secretin. In the latter case the secretion contains entero-kinase, that is to say, is able to digest albumin without the addition of succus entericus.

In this connection it may be mentioned that the use of pilocarpine has led to a physiological understanding of an entirely different kind of secretion, namely, the liberation of a gas. It has long been known that the swimming bladder of fishes contains a gas, the presence of which can hardly be explained by a process of simple diffusion out of the tissues. This fact, which we owe to the observation of Huefner, led Dreser to investigate the process of liberation of oxygen into the swimming bladder of the pike, with a view to determining whether pilocarpine and other glandular stimulants gave rise to an increased accumulation. And indeed he found that when fishes were repeatedly injected with pilocarpine, the content of the swimming bladder in oxygen gas was distinctly greater than in the case of the gas from the normal fishes, which permits the conclusion that the epithelia of the swimming bladder liberate a gas in a manner analogous to the liberation of secretions from true glands, and further that these epithelia are not penetrable in either direction like a diffusing membrane.

Another fact deserves brief notice in this relation. It is the interesting observation of Magnus that when ammonia gas is injected into the veins the alveolar epithelium of the lungs is not penetrable, since no trace of ammonia can be detected in the expired air, whereas after the inhalation of ammonia the gas penetrates readily into the blood through these same epithelial cells. This is merely one striking example of the many known cases in which animal epithelial membranes are penetrable in one direction for certain substances like water, salts or urea, while opposing strong resistance to the passage of these in the opposite direction. The mechanism of this regulatory arrangement has not yet been cleared up and further progress seems hardly possible without the aid of pharmacological methods.

To enter upon the physiology of the heart at this time would carry us too far. Pharmacological facts which have proved of importance in giving us our present knowledge are doubtless sufficiently known to you. We may say, however, that even in regard to the recent controversy over the myogenic and neurogenic theories of the cardiac motions and over the general character of the heart muscle, the systematic study of the cardiac poisons has contributed much that is important

and, as Harnac has indicated, may perhaps furnish the final decision.

Permit me now to direct your attention, for a few moments, to some of the physiologico-chemical results of pharmacological investigations. It lies in the nature of things that the results should be numerous in a field that has to do solely with the chemical inter-relations between the pharmacological agent and the living organism. I shall not tire you with an enumeration of facts already well known. I shall refer only to a few of the more significant biological reactions which we owe to pharmacological investigation. The study of poisoning by acids led to the discovery of ammonia-production in the organism, and this in turn to the Schroeder experiments which positively demonstrated the production of urea in the liver. Pharmacological methods have also contributed materially to the elucidation of numerous other important problems in metabolism. One of the most actively discussed problems has been the question whether sugar can arise from proteid, and this question has been definitely answered, as it seems to me, by the experiments of Rolly. This observer conducted experiments on animals which had been rendered glycogen-free by means of fasting and strychnine spasms. He then brought about an increased destruction of proteids by means of fever, induced through the action of bacteria and toxins, and was able to demonstrate that there occurred a new production of glycogen under these circumstances in the liver and in the muscles. As the fat-reserve of the animals had already sunk to a minimum during the period of fasting, it is clear that the source of the newly-formed glycogen is to be sought in the increased destruction of proteids in the organism. The same sequence of events was demonstrated by Rolly in fasting rabbits at the time of the great destruction of proteids that immediately precedes death.

That the problem of diabetes mellitus, though still unsolved, has received light from many sides through pharmacological investigations, I need hardly state. I will merely remind you that the discovery of phlorhizin diabetes showed us a hitherto unknown capacity of the kidney to secrete sugar, that the work of Lusk and his associates led to the establishment of a definite ratio between nitrogen and dextrose excretion in diabetes, and that Blum and Herter found an adrenalin glycosuria which may perhaps throw some light on the puzzling nervous forms of diabetes.

Again, through poisoning by phosphorus and arsenic the relation of lactic and the amido-acids to the intermediary metabolism was first shown, while as regards the more intimate metabolic processes and their relation to ferment action, the toxicological experiments of Jacobi and of Wakeman have brought us important light. Through poisoning by chloral, by camphor and nitrotoluol, the discovery of glycuronic acid was made, the normal occurrence of which in the organism was only later established. Indeed the various chemical reactions of the organism, of which we have examples in the formation of hippuric acid in the kidneys, in sulphocyanide, in methylation, in oxidation and reduction, were all of them first discovered through the action of chemical or pharmacological agents. Furthermore as regards the location and intensity of these processes, the investigations of Ehrlich and of Herter have given us definite information. I would like to refer here to an interesting observation from Herter's studies which demonstrates with special clearness to the eye the oxygen requirements of the muscles and shows with what energy the muscles appropriate oxygen not only from oxyhæmoglobin, but also from other reducible substances. Herter found that if animals receive intravenous infusions of methylene blue the pectoral muscles were soon colored deep blue, but that if during the experiment the access of oxygen was hindered by giving the animals air mixed with carbon monoxid, the blue muscles in a few seconds recovered their natural red color; they had almost momentarily reduced the methylene blue to the colorless leucobase. It is also known that through the action of hydrocyanic acid the capacity of the organs to take up oxygen from the blood is much reduced or destroyed. This process also it was possible to render easily visible by the method of methylene blue infusion. As we have seen, the pharmacological method has revealed to us a series of functional characters of the organism; but its biological significance appears to extend even further. It seems possible with such methods, if only gradually, to reach a more intimate knowledge of the chemical constitution of protoplasm, and finally, perhaps, to arrive at an insight into the chemical interpretation of its functions. If, under the influence of a pharmacological agent, we observe an immediate essential alteration in the function of a cell, we have to assume that a chemical change has occurred in its vital center—in what Ehrlich has called the "Leistungskern," that is, the chemical center of vital activity. On the other hand if we have before us a gradually developing alteration, this may have been called forth in a secondary manner, through chemical changes in the reserve material or in the supporting elements of the cells, perhaps in the groups of atoms which we conceive as side-chains. Given a knowledge of the constitution and the chemical mode of action of agents operating as acute intoxicants, we should also be able to reach conclusions as to the chemistry of their point of attack, that is to say, regarding that substratum of the living substance which corresponds to the chemical constitution and action of the poison. With a similar idea in mind Oscar Loew, twenty years ago, considered himself justified in assuming the presence of an aldehyde group in the living protoplasm, basing this view on a series of merely qualitative toxic reactions like those obtainable by hydroxylamine, diamid, and other substances.

An example of another pharmacological method which may, perhaps, prove of utility is the investigation of the narcotics. The quantitative comparison of the action of aliphatic narcotics (alcohol, ether, chloroform, etc.) leads to what I believe to be the unavoidable conclusion that certain fat-like substances like lecethin must be conceived as constituting integral parts of the "Leistungskern." It happens that one can compare with considerable exactitude in a quantitative way, the efficacy of this numerous group of bodies.

This comparison has brought out the fact that the degree of activity is approximately proportional to the individual chemico-physical affinities of all these substances, that is, their solution-tensions for fat-like bodies compared with their solution-tensions for watery media. From this almost rigid parallelism it follows with a high degree of probability that in the union of ether, chloroform, etc., to a fat-like substance—a lipoid—we have the origin of the narcosis of the cell; in other words the lipoid belongs to the essential functionally active constituents of the cell. It has been urged against this conclusion that the cell lipoids occasion merely a stronger or weaker accumulation of the narcotic which then acts on the true albuminoid life-center of the cell in proportion to the degree of this accumulation. There are, in reality, only two possibilities. First, one may assume that the narcotic operates only through its presence in lifeless lipoids, whence it acts from a distance, perhaps through a sort of induction, upon the living cell-center itself without entering into reciprocal chemical action with the center. Such a view could be neither refuted nor established. But in order to explain the above-mentioned parallelism, it would be necessary on this supposition to invoke the aid of the very improbable hypothesis that all the different narcotic substances compared on an equimolecular basis, exert an equally strong induction. But this hypothesis wholly fails to allow for the different influence of special groups of atoms, as, for example, the ethyl group, the methyl group, etc. Hence it is clear that such an action at a distance must remain problematical, and furnishes us no actual explanation. On the other hand, we may make the much more likely assumption that the narcotic substance enters into a reciprocal, reversible, chemico-physical action with some constituent of the "Leistungskern" or "life-center," the strength of which reaction is dependent on the intensity of this reciprocal action. Then again, the law of mass action here comes into play, that is the law of distribution. We may even leave the lipoid for the moment out of account. In this case it would have to be regarded simply as an intermediary solvent and would remain without influence upon the equilibrium established by the narcotic between the blood and lymph plasma on the one hand and the "Leistungskern" or "life-center" on the other. Experiment, however, showed that the affinity of the living cell substance for a narcotic, measured by the observed intensity of action, runs parallel to the experimentally observed fat affinity of the narcotic, or, in other words, that the unknown constituent of the living cell or "Leistungskern" must itself possess certain properties of a fatty substance, or, in short, must itself be a fat-like or lipoid body. And thus we come back to the very conclusion of which I have already spoken. I have expressed myself in somewhat greater detail than is perhaps warranted by the importance of the question. I have, however, thought such a critical discussion of the problem of some interest as it seems of fundamental significance for the evaluation of a pharmacological analysis of this kind.

I have already said that perhaps the highest result of pharmacological investigation may prove to be the winning of an insight into the chemical nature of life processes themselves; indeed, the first important ground in this direction has already been won. You are all familiar with the important investigations of Jacques Loeb, to whom we owe a knowledge of the essential significance of the individual metallic ions, for the general life processes. But what is still more important, Loeb has succeeded in inducing very special biological reactions as the effect of chemical action. He has shown that heliotropism can be excited by definite chemical reagents such as carbon dioxide and other substances, instead of through the action of light, which is a contribution to the understanding of the mechanism of this singular reflex function. Finally, he has shown that through certain definite chemical procedures like the action of hypertonic salt solutions, combined with ethyl acetate, the unfructified eggs of sea-urchins may be stimulated to parthenogenetic normal development, an observation which may prove of great significance for the understanding of the process of fertilization.

And with the mention of this admirable investigation, permit me to close my address of to-day.

OBSERVATIONS ON SEVERAL CASES OF ACUTE PANCREATITIS.

By William Sydney Thayer, M. D.,

Professor of Clinical Medicine in the Johns Hopkins University.

The following cases, four of which come under the head of suppurative, and one of gangrenous pancreatitis, are deemed worthy of report, as well from a diagnostic standpoint as from the fact that their course and outcome emphasize the importance of early recognition and prompt surgical interference under similar circumstances. The first of these cases was seen a few months ago in consultation with Dr. J. C. Pound. The other four are from the wards of the Johns Hopkins Hospital. Three of these I have had the good fortune to see myself; one was under the care of Dr. Futcher.

Case I. *Woman; 51. Previous attacks of biliary colic. Onset of present illness with an attack of biliary colic and jaundice followed by fever, nausea, vomiting, and pain on the left side of the abdomen. Deep tumor mass occupying the epigastrium and left side of the abdomen, extending well out-*

ward and backward into the flank. Operation, thirty-seven days after onset, revealed parapancreatic abscess with disseminated fat necrosis. Recovery.

Mrs. W., married, 51 years of age, was seen in consultation with Dr. J. C. Pound on 31 October, 1904. The *family history* was negative. She had had typhoid fever in childhood but had otherwise been a healthy woman. Married; no children. Passed the menopause a year ago. Ten years ago had a few attacks of sharp pain in the epigastrium and right hypochondrium seldom associated with nausea or vomiting.

Present Illness.—In June she had had a sharp attack of pain in the epigastrium and right hypochondrium lasting several days; this was associated with jaundice which lasted a week. The stools, for several days, resembled putty. Four weeks ago to-morrow the patient had another attack of pain in the epigastrium of not very marked severity, though it was enough to require an hypodermic of morphia. This was followed by jaundice which lasted four or five days. There was also fever and nausea and vomiting which, at first, were rather severe. There was what she calls a "sore pain" in the epigastrium, particularly on the left side. The nausea and vomiting, worse in the afternoon, have continued off and on ever since. There has been intermittent fever associated with considerable sweating at times, especially at night. The main complaint has been of a "sore pain" throughout the left side of the abdomen.

On *physical examination* the patient was found to be a well-nourished woman of a rather sallow, yellowish appearance, suggesting suppuration; temperature 102.8°. The thorax was clear throughout, the *lungs* descending behind to an equal level on both sides. The *heart* sounds were clear; the apex in normal position. The *abdomen* was rather full, slightly more prominent on the left side, especially a little above the crest of the ileum. On palpation there was to be felt a deep mass extending somewhat across the epigastrium to the right but especially filling up the left side of the epigastrium, and extending downward to a point as low as the level of the anterior superior spine of the ileum. On the left it reached to a point about as far out as the mid-axillary line. It was deeply situated below the gut. The border of the *liver* was not clearly felt and on the right did not, apparently, descend below the costal margin. The mass suggested to Dr. Pound and myself a deep parapancreatic abscess, although the situation was much further to the left than is common in such cases. The relation of the symptoms to the attack of biliary colic was, however, suggestive.

1 November. Examination of the blood showed: red blood corpuscles, 3,964,000 to the cu. mm.; colorless corpuscles, 16,800 to the cu. mm.; hæmoglobin (Dare) 61%.

A differential count of 500 leucocytes stained by Ehrlich's method showed: small mononuclears, 8.6%; large mononuclears and transitionals, 6.6%; polymorphonuclear neutrophiles, 84.4%; eosinophiles, 0.4%; mast cells, 0.4%.

The red cells were normal in size and form. There were no irregularities in contour; no nucleated red corpuscles were observed.

Urine.—Normal, amber color, clear, acid 1009, no albumin, no sugar. Microscopically, few squamous epithelial cells; an occasional leucocyte; no casts; no crystals.

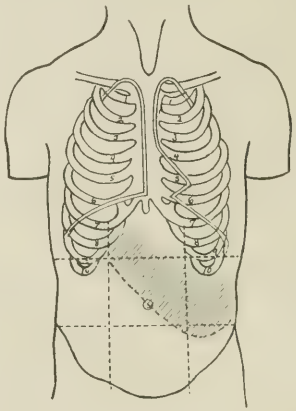
An exploratory operation was suggested, but the family demurred.

7 November. On this date the patient was again seen in consultation with Dr. Pound. During the past week the condition has not essentially changed. Examination to-day, however, shows some slight modification in the character of the mass which extends, perhaps, a little lower, while it is not as prominent in the epigastrium. There is, also, flatness in the left back, reaching to a point as high as the angle of the scapula. The upper limit of dulness is higher in the scapular line than at the spine. In front, however, the lower level of the lung is about at the same point as on the right. Below the line of flatness, vocal fremitus is absent, while the respiration is rather indistinct, of a tubular quality, with nasal voice sounds, somewhat suggestive of ægophony, especially toward the upper part.

9 November. The patient who had been urged to consent to operation, agreed to see Dr. Finney to-day. On examination a decided change was noticed in the outline of the deep mass, in that it projected much more in the flank, reached further outward and began to show distinct evidence of fluctuation. There was also slight œdema of the subcutaneous tissue just above the crest of the ileum.

The patient was removed to the Union Protestant Infirmary where Dr. Finney operated on the following day.

The abscess was opened in the left flank where it appeared to be pointing. This opening led into a very large cavity which extended upwards into the epigastrium in the region of the pancreas, downwards toward the pelvis and backwards into the para-renal region. Escaping with the pus were masses of necrotic fat and shreds of necrotic tissue.



Position of deep mass in Case I.

The patient bore the operation well, but the fever, ranging from normal in the morning to 100° and 101° at night, continued. There were frequent attacks of nausea and vomiting; little food could be retained. On 20 November, I saw the patient who was much emaciated, extremely feeble and delirious. The pulse was 140. The condition was such that it was feared she might not live through the night. From this time on, however, she steadily improved. The vomiting ceased, the appetite returned and the delirium disappeared.

On 22 December, the patient had so far improved that she was able to go home, although the evening temperature was still a little above 99° while a sinus persisted.

The *urine* was free from sugar throughout.

In the discharge from the wound large masses of necrotic tissue appeared on various occasions. On 20 November, for instance, a piece measuring 6 x 6.5 cm. escaped, while on 29 November, a piece was discharged as large as the palm of the hand.

Several of these masses suggested bits of true pancreatic tissue.

A specimen was sent to Dr. Bloodgood who made the following report:

Pathological No. 5897. Mrs. W., patient of Dr. Finney, U. P. I.

"*Clinical Diagnosis, Pancreatic Abscess.*—Necrotic and hæmorrhagic tissue shows no evidence of remains of pancreatic gland.

Gross Description.—The specimen consists of a mass of tissue which is so friable and mushy that it cannot be handled without falling to pieces. It is of a greyish pink color and seems to be somewhat loosely bound together by fibrous shreds; in one area there is a blackish mass, quite friable, which has the appearance of a blood clot.

Microscopical Description.—Section 1, marked 'blood clot,' shows areas of disorganized blood in a granular tissue taking the eosin stain in which I can recognize no stained nuclei. The architecture of the necrotic tissue suggests fat.

Section 2, marked 'tissue' has the same appearance as section 1, no nuclei taking the stain. There is no tissue suggesting the architecture of fat and no positive evidence of pancreatic tissue.

Remarks.—Clinically, the case was considered by Dr. Thayer to be one of pancreatic disease. The tissue sent to the laboratory was of necrotic hæmorrhagic fat which came from the abscess cavity."

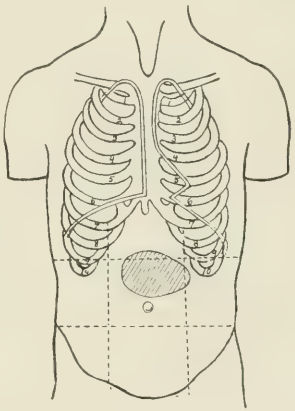
Case II.[1] *Man; 34. For a year and a half attacks of cramp-like epigastric pain; present attack: severe epigastric pain; vomiting; fever; epigastric tumor; diagnosis of acute pancreatitis with parapancreatic abscess; operation twelve days after onset; recovery.*

Hosp. No. 10,210; Surg. No. 3190. W. E. D.; aged 34; married; a piano polisher, was admitted to the Johns Hopkins Hospital on 25 June, 1905. *Family history*, negative. *Previous History.*—As a child had had chicken pox and pneumonia, the latter at the age of six. Had been married thirteen years; no children. For years had been a regular drinker of beer and whiskey though not to great excess. Smoked and chewed tobacco. Five years before entry had been overcome by heat. Was in bed at this time for a week. For two years had been subject to attacks of nausea in the morning with occasional attacks of vomiting, the vomitus consisting of a greenish, slimy substance.

For a year and a half the patient had been subject to attacks of severe cramp-like pain in the abdomen. The pains were localized in the median line across the epigastrium and about the umbilicus. The first attack came on at night and was very severe, so much so that relief was obtained only by large doses of morphia. With each attack the patient had been compelled to remain at home for from several days to a week. There was often vomiting; probably fever; never jaundice.

P. I.—Ten days before entry the patient came home from work on account of a slight sensation of heaviness in the epigastrium and a feeling of anxiety similar to that which had preceded his other attacks of pain. The same evening vomiting came on. The pain was intense and continuous, and a swelling appeared just above the umbilicus at the area of greatest tenderness. There was constipation. During the next week the patient was obliged to remain in bed. There was continuous fever, and delirium. A diagnosis of abscess of the liver was made by his physician. On 25 June, he was admitted to the Johns Hopkins Hospital. I saw the patient shortly after entry and made the following note:

"On physical examination the patient is a well-formed man, quite corpulent; lips and mucous membranes of good color. The tongue is coated, the temperature elevated; the mental condition dull; the patient is a little confused. Examination of the *thorax* is negative. On inspection the *abdomen* is full, showing a rather undue prominence in the median line across the epigastrium. Hepatic flatness begins at the sixth rib in the mamillary line, while in the same line the lower border of the liver can, apparently, be felt about on a level with the umbilicus; it is not, however, very distinct, owing to the tension of the abdominal muscles. Liver-flatness is coextensive with this area. Passing toward the median line the resonance becomes tympanitic. Just below the xyphoid cartilage the resonance is loudly tympanitic, and from the sensation conveyed by palpation there is evidently an air-containing organ (stomach?) just below the skin. Below, between this and the umbilicus, at the point of maximum prominence, is to be felt a deeply seated mass, over which there is well marked tympany. The outline of the mass is indistinct. It is not tender on ordinary palpation. To the right this mass is not to be sharply separated from what would appear to be the liver; to the left it reaches about to the costal region. Pressure over the lower left ribs does not cause pain. In the knee-elbow position nothing further is to be made out. *Splenic* dulness is about normal in area, and does not pass the costo-articular line. There are no glandular enlargements." The appended chart, made at the time of this examination, shows the position of the deep mass, of the hepatic dulness, and the epigastric tympany.



Position of the palpable mass in Case II.

The *urine* was free from albumin or sugar.

The *blood* showed a leucocytosis.

A diagnosis of acute pancreatitis with disseminated fat necrosis and, possibly, sequestration of the pancreas was made, and an exploratory operation was advised. This was performed by Dr. Finney on 27 June.

In the median line, adjoining the liver and stomach, a mass of adherent fatty tissue was found which was filled with numerous fat necroses. This mass of tissue was adherent to the stomach and liver. The transverse colon passed over the lower part of the opening and was involved in the adhesions. The general abdominal cavity was packed off with gauze and an opening into the mass was made later. From this opening a large quantity of brownish pus with large masses and shreds of necrotic fat escaped. The finger passed far backward at the bottom of the wound into what appeared to be a cavity in the pancreas. The main excavation represented evidently the lesser peritoneal cavity. The material discharged from the opening showed pus, bacteria, numerous fatty acid crystals and large and small masses of

[1] Published previously in the Am. J. M. Sc., Phila, 1895, CX, 396.

necrotic fat. Cultures were unfortunately not made, as the opening occurred unexpectedly. No tissue that could be definitely identified as pancreatic was found in the discharge. The patient made a perfect recovery and has been well ever since. His present good health may be inferred from his appearance, for he has kindly consented to come before us this evening.

CASE III.[2] *Man, 47; six months before attack, jaundice with biliary colic; present illness: sudden intense cramp-like abdominal pain; nausea; vomiting; collapse; abdominal distension; constipation; tender, painful tumor in the right half of epigastrium and hypochondrium; diagnosis by Dr. Bloodgood of pancreatitis; operation on 21st day; death; necropsy; necrosis of pancreas; suppurative parapancreatitis; stone lodged in diverticulum of Vater.*

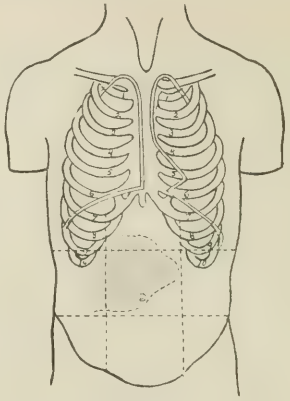
Hosp. No. 30,996; Med. No. 11,482. J. T. H.; 47; married; physician; entered the hospital on 26 June, 1900, complaining of abdominal pain, distension and fever.

The *family history* was negative. *Previous History.*—Has had scarlet fever and measles. Chews tobacco; does not smoke or drink; is not a heavy eater. Has complained frequently of pain and distension after eating; rarely, nausea and vomiting.

Six months ago, had an attack of jaundice accompanied by slight pain in the abdomen; the jaundice lasted for several weeks. During this period the stools were but slightly clay-colored. His sister is inclined to believe that this attack was not dissimilar to his present illness. There was some nausea and a good deal of abdominal pain; moderate fever. He was obliged to stay in bed for some time, but by the end of three weeks had recovered entirely.

Present Illness.—Eighteen days ago, at nine o'clock at night, there was a sudden attack of nausea and vomiting with intense cramp-like abdominal pains which could not be localized. The patient was collapsed, the abdomen distended, and the pain rather general; no change in the condition for four or five days. On the third day the patient was found to have a temperature of about 101.5°. After the first night the vomiting became less frequent though it has occurred off and on ever since. The bowels were constipated, possibly due to the morphia which was given; the skin, cold and clammy. The respirations were not accelerated. On about the seventh day a tender area was noticed in the right hypochondrium which was a little fuller than any other part of the abdomen, though at no time during the illness were the muscles of the right side more rigid than those of the left. The physician believes that the abdominal respiratory movements were practically normal. On the fifth day the bowels were opened by purgatives. The fæces were normal in color and have been essentially natural since then, although laxatives have had to be used twice. The last movement occurred four days ago. For eleven days there has been an irregular fever ranging between 101° and 103°; there have been four or five chills. Nausea and vomiting have been slight and the abdominal pain has not been severe. But little morphia has been given. The area of tenderness in the right hypochondrium has, however, persisted, while the abdominal distension has steadily increased. There have been no cerebral symptoms, and the mind has been perfectly clear throughout. There has been no jaundice. The patient has lain on his right side during most of the time, with the thighs flexed on the abdomen. The pulse has ranged from 100-120; at times, dicrotic.

26 July, 1900. On entrance, the patient was seen by Dr. Futcher who made the following note: "The patient is a man of large frame; complexion, a trifle sallow; mucous membranes, somewhat anæmic; tongue, a little coated; very slight yellowish cast to the conjunctivæ. He lies upon his right side with the knees flexed. The pulse is of fairly good volume and tension, regular in force and rhythm, vessel wall not thickened. *Lungs*, clear throughout on percussion and auscultation. *Heart.*—Point of maximum impulse not seen or felt. Sounds best heard in the fourth interspace, 9 cm. from the midsternal line; sounds enfeebled at apex and base. *Abdomen.*—The right costal groove is partially obliterated; the right lumbar region slightly fuller than the left. There is a distinct, visible prominence in the right hypochondrium and the right half of the epigastrium, extending into the upper right quadrant of the umbilical region. Distinct pulsation is visible in the upper epigastrium. Respiratory movements are less marked on the right than on the left. On palpation there is a distinct resistance in the area above noted. The lower margin of this area of definite resistance corresponds with the line indicated in the chart extending a little to the right of the umbilicus to a point about on a level with the anterior



Position of palpable mass in Case III.

superior spine, passing up through the umbilicus, the left border of the umbilical region and around again through the epigastrium to the right. To the right the outline of the mass is not so easily felt. The margin is rather round and extends to a point 10.5 cm. below the costal margin in the mamillary line and to the level of the umbilicus in the median line.

The surface is firm, a little irregular. The lower margin descends on inspiration. In the median line the fingers can be pressed in above the resisting mass. There is dull tympany over the tumor and the dulness is continuous above the costal margin with the hepatic flatness which extends to the middle of the sixth interspace. . . . The border of the spleen is not definitely felt. There is nothing to be made out in the right iliac fossa." Leucocytes 18,300.

27 June, 1900. The stool passed last night was soft, unformed, golden in color throughout, rather resembling gold dust and having a definite glistening appearance. There was nothing remarkable save for the large number of fatty acid crystals.

Following inflation of the stomach with tartaric acid and bicarbonate of soda, the epigastrium and upper part of the umbilical region became decidedly more prominent. There was no peristalsis. The upper border of the stomach tympany began over the middle of the sixth interspace in the parasternal line

[2] This case has been reported by Dr. Opie in Am. J. M. Sc., 1901, CXXI, 27.

and reached a point 5.5 cm. above the level of the umbilicus in the median line. The stomach, after inflation, measured only 21 x 11 cm. The mass in the right hypochondrium and right half of the umbilical region did not appear to be connected with the stomach. The glands in the left axilla were slightly enlarged. Leucocytes, at 11 a. m., 19,300. The condition was about the same. There was some nausea and vomiting early in the morning. The vomitus was green in color, acid to litmus. Free hydrochloric acid was present, the acidity amounting to 27; total acidity, 50.

Urine.—High; clear; acid; 1017; no sugar; trace of albumin. Microscopically: mucous cylindroids; one granular cast seen.

28 June, 1900. Leucocytes, at 4 p. m., 19,500. There has been no change in patient's condition. He takes his nourishment well and has not vomited since yesterday. The temperature, since admission, has ranged between 99.2° and 101.8° and but once has been above 100.4°. He has complained of no pain and there is but little sensitiveness on palpation over the mass. The patient has, at times, been somewhat irrational and very drowsy. The right lateral decubitus and the flexion of the knees and thighs continues. There is no muscle spasm. The pulse has varied from 108-124, and has, at times, been irregular and intermittent. The respirations since admission have been from 20-28 to the minute. A fresh specimen of blood shows nothing abnormal save a leucocytosis, chiefly polymorphonuclear.

29 June. 6 a. m., leucocytes, 18,500. Last night the patient was decidedly irrational; the pulse, irregular and rapid. There was marked restlessness, the patient endeavoring to get out of bed. The temperature rose during the night reaching 104° at six this morning. Stool, obtained by rectal tube, showed no amœbæ; no red blood corpuscles; no pus. Color, light yellow; a few fatty acid crystals. The stool early this morning was liquid, of a yellow ochre color; no amœbæ; no blood corpuscles; no pus. There was a large quantity of fatty acid crystals; no fat globules.

Dr. Futcher made the following note: "The mass in the right hypochondrium and epigastrium has not apparently changed in size. There is no tenderness on palpation." The temperature rose at six p. m. to 104°. The *urine*, throughout, was free from sugar.

The patient was seen on this date, by Dr. Bloodgood, who made a diagnosis of suppurative pancreatitis and advised operation which was performed on the following day. On opening the peritoneal cavity numerous areas of fat necrosis were visible. The omentum was matted together. On making an opening through the omentum a large amount of dark, brownish black fluid escaped. The patient's condition was so bad that a drainage tube was inserted and the wound closed without further investigation. The general weakness, however, increased and at 8 p. m. the patient died.

Necropsy.—Anatomical diagnosis; cholelithiasis; calculus lodged in the common duct near its orifice; slight jaundice; old hæmorrhage within and about the pancreas; localized necrosis of pancreas; chronic interstitial pancreatitis; necrosis of fat of pancreas; greater and lesser omentum, mesentery and subperitoneal tissue of the abdominal wall; parapancreatic abscess limited by lesser peritoneal cavity; laparotomy wound.

A partial necropsy was made by Dr. Opie through the incision three hours after death. "The body is that of a large-framed, muscular man with abundant subcutaneous fat. *Peritoneal Cavity.*—The omentum, which contains a large quantity of fat, is adherent in the neighborhood of the operation wound to the anterior abdominal wall by light, fibrinous adhesions. Its surface is thickly studded with conspicuous, opaque, white areas, varying in size and shape, but usually round and about 3 mm. in diameter, extending about 1.5 mm. below the surface. On section similar foci are found embedded in the fat. Opaque, white areas are present in the fat of the mesentery, where they are most abundant near its intestinal margin, in the subperitoneal fat of the anterior abdominal wall, over the bladder, over the kidneys, and about the colon. *Abscess cavity.*—The drainage-tube inserted into the abdominal wound passes through a small, incised opening in the great omentum and enters an immense abscess cavity which occupies approximately the site of the lesser peritoneal cavity. The foramen of Winslow is closed. The stomach is pushed upward and forward, and its anterior surface is adherent to the lower surface of the liver to the left of the gall-bladder. The spleen, partially surrounded by fat containing many opaque, white areas, is bound by fibrous adhesions to the diaphragm. The walls of the cavity are very irregular and ragged, and have a necrotic appearance, in general opaque and gray, occasionally black. This blackish-gray appearance extends only a short distance below the surface, and where the wall is formed by fat, give place to numerous foci of opaque, white color. The retroperitoneal fat in front of the left kidney and psoas muscle has been eroded, and an extension of the cavity passes behind the jejunum near its junction with the duodenum. To the left of the descending portion of the duodenum, occupying the position of the pancreas and projecting forward into the abscess cavity, is a great mass of black material, necrotic in appearance, extending to the left as far as the spleen. This material is reddish-black on section, somewhat spongy in texture, soft, dry, and friable. The cavity contains a large quantity—at least 500 cc.—of fluid, reddish gray material, containing fat droplets and black, necrotic particles. The *bile ducts* are slightly dilated and contain thin yellow bile. The *gall bladder* is bound by numerous adhesions to the duodenum and stomach. Its walls are thickened and it is much distended, containing viscid yellow bile and a large number—over one hundred—of brown facetted calculi varying in diameter from 0.5 to 1 cm. The hepatic, cystic and common ducts are much dilated. On opening the duodenum a stone is felt below the mucous membrane situated in the common bile duct, about 1.5 cm. from the orifice of the diverticulum of Vater. It is 7 mm. in diameter and resembles those present in the gall bladder.

Pancreas.—The pancreatic duct unites with the common bile duct at a point 7 mm. from the duodenal orifice. For a distance of 1.5 cm. the two ducts are separated by a thin septum only, and in contact with this septum is lodged the gall stone previously mentioned. The pancreatic duct is not distended. The pancreas occupies the posterior wall of the lesser peritoneal abscess cavity, and is covered by the mass of reddish black, friable material, changed, coagulated blood, above described. The organ is of large size, and the glandular tissue is in great part firm, yellowish-white, and well preserved. The interstitial tissue has a dull, reddish, in places hemorrhagic appearance, and contains conspicuous, opaque, areas of irregular shape. Where the anterior surface of the head and body is in contact with the overlying material there is a superficial zone of soft, grayish, necrotic appearance.

The other organs—*heart, lungs, spleen, stomach, intestines,* and *kidneys*—present no noteworthy alteration. . . . "

The complete histological examination may be found in Dr. Opie's article above referred to.

Bacteriologically, cultures from the heart's blood, lungs and liver showed *bacillus coli.* A plate culture from the material covering the pancreas and forming part of the abscess wall contained the *B. coli* and the *B. lactis aërogenes* and the *B. proteus.*

Case IV. *Woman; 49. Previous attacks of biliary colic; sudden severe epigastric pain relieved by morphia; persistent dull epigastric pain with nausea and vomiting; tender tumor in the right umbilical, epigastric and lateral abdominal re-*

gions; diagnosis by Dr. Halsted of pancreatitis; operation; recovery.

Hosp. No. 39,822; Med. No. 14,390; Surg. No. 13,415. V. C. B.; single; 49; housekeeper; a patient of Dr. J. T. Strickland of Roanoke, Va., was admitted on 20 May, 1902, complaining of "stomach trouble."

Family history.—Negative. *Previous history.*—Patient has had measles, chicken pox, and whooping cough and, fifteen years ago, typhoid fever. Passed menopause five years ago. Has been subject to severe headaches; has never suffered from digestive disturbances until four years ago when she was suddenly seized with an agonizing pain in the pit of her stomach; the pain did not radiate; it continued until relieved by morphia. There was no nausea or vomiting but she felt cold and sweated profusely; no jaundice. From that time she has had occasional similar attacks but they have not increased in frequency in the past year, and she has always recovered on the following day.

Present illness.—Five weeks ago the patient had a sense of discomfort in the epigastrium after eating supper; this distress became gradually worse, and, in about four hours, had developed into an agonizing pain in the pit of the stomach. The pain did not radiate into the back. She was cold; there was a drenching sweat but no nausea or vomiting; no jaundice. Hot applications gave no relief, which was afforded only by an hypodermic injection of morphia. The attack was similar to those which she had had previously, but more severe. Ever since this time she has felt very ill. There has been constant dull pain in the epigastrium; attacks of vomiting, persistent and protracted, have recurred every two or three days, the vomitus being thick and dark green in color. She has been able to take only very light food. At the onset there was obstinate constipation for about a week; thinks she has had a little fever every now and then toward night. There have been no chills; no sweating at night. There has been no attack of sharp pain since the onset. About three weeks ago she noticed a hard tender mass in the abdomen which has not disappeared. She has never been jaundiced; has been extremely nervous and has not slept well.

On the day of entry the blood count showed: red blood corpuscles, 4,120,000 to the cu. mm.; colorless corpuscles, 8250 to the cu. mm.; hæmoglobin, 68%.

On the same day the following note was made by Dr. Thayer: "The patient is sparely nourished; lips and mucous membranes of good color; the skin is slightly yellow; the sclera pure white. The temperature last night was 100.5°, this morning 99.2°. Pulse 31 to the quarter, of moderate size, fairly good tension; vessel wall, not palpable.

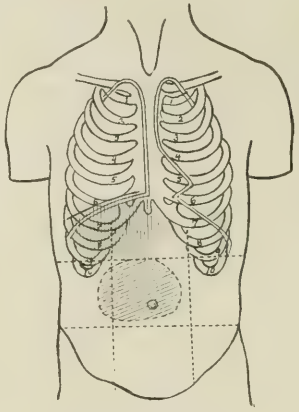
Thorax symmetrical; costal angle about 90. Expansion equal. Resonance clear in fronts and axillæ. *Heart.*—Apex impulse in the fifth space in normal position; sounds clear, of normal relative intensity.

The *abdomen* looks a trifle fuller in the right epigastric and umbilical regions than on the left. No observable peristalsis. On palpation, there is to be felt a firm, very tender mass which lies in the epigastric and right umbilical regions extending over into the right lateral abdominal region. This descends to a point slightly below the level of the umbilicus and moves downward slightly with inspiration. It has, so far as can be made out, no sharp border. To the right the outline is indistinctly to be felt passing a little beyond the vertical line extending through the anterior superior spine of the ileum. To the left it reaches apparently about 3-4 cm. beyond the umbilicus. The hepatic flatness passes directly into the dulness over the mass but the dulness is not absolute. Even on light percussion there is slight tympany over the tender area. The spleen is not palpable though there is dulness to the costal margin as indicated on the chart. The border of the mass has not the sharp edge of the ordinary hepatic border though it does feel rather firm. There is no apparent fluctuation. Below this area the abdomen is negative. There is no prominence in the right lumbar region. The tumor mass is not to be felt with the posterior hand over the lower ribs. Without dilatation it is impossible to differentiate the stomach from the other air-containing organs. As the patient changes position the tumor is practically immobile, falling but little toward the dependent side."

The *urine* was of normal color; acid; 1017; no sugar; trace of albumin. Sediment, flocculent containing a few hyaline casts, mucous cylindroids and epithelial cells. No Diazo reaction. The Widal test was negative.

The temperature during the two days that she was on the medical side, ranged between 99.2° and 100.2°. Nothing remarkable was noted about the character of the *fæces*, no entry being made in the history.

On the following day the patient was seen by Dr. Halsted who regarded the case as one of pancreatitis and advised operation, which was performed by him on 23 April. An incision was made over the mass in the right hypochondrium, through the rectus muscle and separating the fibers. When the peritoneum was reached there were some œdema and evidence of inflammation. The peritoneum was divided and the abscess cavity was immediately encountered, from which about an ounce of thick, yellow material was evacuated. This was odorless and contained numerous small masses resembling fat. The opening was enlarged a little and the cavity explored. It ran downward for a distance of about 7 cm. and backwards perhaps 10 cm. It appeared to be lined on the sides by bowel and posteriorly by a hard mass, the exact position of which could not be determined. The abscess cavity contained masses of necrotic looking tissue which Dr. Opie regarded as necrotic omental fat. A considerable quantity of this necrotic stringy material was evacuated and the abscess cavity was wiped out and packed with iodoform gauze. . . . The abdominal cavity was not opened and no exploration was made to determine the presence or absence of gall stones. The patient made an uninterrupted recovery and was discharged from the hospital on 24 June well.



Position of tumor in Case IV.

Case V. *Man; 37. Seven months before entry, intense epigastric pain; vomiting and purging; gradual recovery in*

two months; three weeks before entry, epigastric pain; vomiting; persistence of symptoms in a milder degree; diagnosis of pancreatitis; operation; death from hæmorrhage into cavity; necropsy: gangrenous pancreatitis; perforation of stomach and duodenum.

Hosp. No. 43,308; Med. No. 15,860; Surg. No. 14,924. S. T. H., married, 37 years old, mechanic, patient of Dr. Jones of Newbern, N. C., was admitted on 7 July, 1903, complaining of pain in the stomach, nausea and occasional vomiting.

The *family history* was negative. *Personal history.*—The patient had chicken pox at 9, measles and whooping cough at 10; malarial fever at 24; occasional attacks of "kidney colic." He was married at 31. His wife had had no children and no miscarriages. Had been a hard worker, his occupation keeping him indoors most of the time. Had not been a heavy drinker but occasionally drank apple brandy. Had been a hearty eater; a slight smoker; had chewed a good deal of tobacco; denied venereal disease.

Present illness.—Seven months before entry he was seized at night with a sudden severe pain in his stomach associated with vomiting. The pain which had improved, returned in the morning and continued most of the day associated with moderate purging. The vomitus contained no blood. The pain lasted off and on for two months but finally entirely disappeared. His health remained fair up to three weeks ago, when he had another attack of pain in the stomach associated with sweating and moderate vomiting. There was no jaundice; he was somewhat constipated. The bowels were moved by purgatives. He had weighed 185 pounds, but lost much with his first attack after which, however, his weight returned to 172 pounds. It now is about 160. During the last three weeks he has grown much weaker. At one time a tumor is said to have appeared in the gall bladder region which was lifted by the heart beat and pulsated. It has, since then, disappeared entirely. On the day of entry the following note was made by Dr. Thayer: "Complexion very sallow, conjunctivæ clear, slightly, if at all, yellow. Tongue, dry with a yellowish coat; clear and pale on the edges. Complexion, very dark. Patient looks ill; the eyes are sunken; pulse 29 to the quarter at the beginning of examination; size moderate, rather compressible.

Thorax.—Symmetrical; costal angle, 90. Note over the right lung seems slightly more tympanitic than over the left. Flatness begins on the right side at the sixth rib in the mamillary line; on the left at the lower border of the seventh. Respiration is clear in the left front and axilla; also in the right front. The lower border of the left lung behind is a trifle lower than that of the right. Back is clear on auscultation.

Heart.—Negative. *Abdomen.*—Natural. Well marked epigastric pulsation. The left side of the epigastrium is slightly fuller than the right. On palpation there is to be felt a distinct muscular resistance in the epigastrium more particularly on the right side. The *liver* is rather indistinctly felt. It descends on deep inspiration, from under the ribs, in the anterior axillary line. Under the superior belly of the right rectus there seems to be something which descends with inspiration but the tenseness of the muscle prevents accurate palpation. In the median line also there is a distinct tenderness but nothing very definite is to be felt. The gastric resonance is easily made out extending rather far to the right and lying rather transversely. The *spleen* is not distinctly palpable though the dulness just passes the costo-articular line. In the median line the liver dulness reaches one and a half finger's breadths below the tip of the ensiform.

A little later Dr. Cole observed that the patient looked very ill and was in a rather collapsed condition. The abdomen was a little full, especially in the upper half, more so on the left side of the epigastrium than on the right. Well marked epigastric pulsation. On the right movements are fairly good. "On palpation, below the umbilicus, the walls are not held firmly, and fairly deep palpation may be made without much resistance. No masses are palpable. There is a marked increase in resistance above the umbilicus and in the epigastrium. Here there is very distinct tenderness though it is not exquisite, and the walls are held quite firmly, the patient resisting voluntarily; there is no definite muscle spasm. On deep inspiration one can make out an indefinite mass in the epigastrium, the lower border of which is felt extending across the median line about midway between the umbilicus and the tip of the ensiform and reaching upwards to the left costal margin. This ridge feels somewhat irregular though it cannot be definitely determined. The percussion note over this mass is tympanitic; it lies apparently behind the stomach. No mass is felt in the right hypochondrium. The edge of the liver is not palpable."

The temperature was normal, ranging during the few hours that he was on the medical side, between 97.6° and 98.6°.

A blood count showed: red blood corpuscles, 5,140,000 to the cu. mm.; colorless corpuscles, 33,700 to the cu. mm.; hæmoglobin, 82%.

An approximate hasty differential count showed in one hundred cells: small mononuclears, 6; large mononuclears, 5; polymorphonuclears, 89; eosinophiles, none.

The *gastric contents*, after an Ewald test meal, amounted to 22 cc. of a fluid of a bright green color with flaky particles. The supernatant fluid is opalescent, the odor characteristic; total acidity, 33; hydrochloric acid, 19; no lactic acid. Microscopically: Bacilli of various kinds, no Oppler-Boas bacilli; many cells, for the most part leucocytes; few epithelial cells and yeasts.

Urine.—Yellowish brown; slightly turbid; 1022; strongly acid; no sugar; no albumin; urea 0.33 per cc.; no bile pigment; sediment: uric acid; two doubtful hyaline casts in centrifugalized specimen.

A diagnosis of acute pancreatitis was made and the patient was transferred to the surgical side, Dr. Finney performing an exploratory laparotomy on the same day. The peritoneal cavity contained no free fluid. The omentum seemed rather hard and indurated; no fat necrosis. The gall bladder was found to be rather thick but no stones were palpable. The tip of the omentum was adherent far down on the right side just below the gall bladder, and at this point there were two areas which looked like spots of fat necrosis. A number of similar points about one or two cm. in diameter were also found in the mesentery of the ascending colon. There was some general thickening of the pancreas which was most marked at the tail where there was a good sized mass. The spleen was large and surrounded by adhesions. The liver seemed small. The case was considered to be one of acute pancreatitis or possibly carcinoma of the tail of the pancreas and it was deemed inadvisable to explore further.

9 July, 1903. The patient's condition after operation was fairly good. In the evening the temperature was 104°, falling the next morning to 101.8°, the pulse improving correspondingly. To-day, however, the pulse has been weak, about 120, and strychnine and digitalin have been continued. In the afternoon the temperature rose to 102.3°. The patient began to wheeze, cough, and expectorate, and in the left side of the chest, both in front and behind, loud moist rales were heard; no tubular breathing.

11 December. The patient's condition grew steadily worse. There was frequent vomiting which was not relieved by washing the stomach. The pulse was weak and rapid. The abdomen was not distended. The temperature on the 10th ranged from 100.8° to 102.6°. On the afternoon of the 11th there were three profuse discharges of fresh bright blood from the bowels, death following soon afterwards, at 4 p. m.

Necropsy (*No. 2135*). *Anatomical diagnosis.—Acute gangren-*

ous pancreatitis with necrosis of the greater part of the pancreas; formation of fat necroses and perforation of stomach, duodenum and transverse colon; erosion of splenic artery with hæmorrhage into the pancreas and transverse colon; cholelithiasis; arterio-sclerosis of coronaries.

A partial necropsy was performed through the incision which was slightly enlarged. The *peritoneum* in the region of the incision showed a few ecchymotic areas. The great *omentum* was well developed and was slightly adherent to the hepatic flexure of the colon. The *cæcum*, *ascending* and *descending colon* were of a deep red color. . . . The *spleen* was adherent to the diaphragm and a mass could be felt in the region of the tail of the *pancreas*. On dissection between the *stomach* and *transverse colon* in the median line, a cavity was opened containing a dark red mass of semi-fluid blood clot mixed with a number of opaque, white, firm, friable masses. These masses possessed no definite structure but it was possible to see that at one time they probably had had an alveolar arrangement. There was a fæcal odor. The abdominal organs were removed entire and on cutting through the *œsophagus* a few small blood clots escaped. In tearing through the adhesions between the spleen and the diaphragm another cavity containing similar material was opened; this proved to be continuous with that which was first described. On careful examination of the transverse colon an opening was found in its superior surface 1.5 cm. in diameter with fairly smooth edges. This was situated about 5 cm. to the right of the middle line. The mucosa of the colon in this region was deeply blood-stained as well as the surrounding tissue in the cavity wall. The stomach was now opened along the greater curvature; a small quantity of slightly reddish fluid escaping with a few of the opaque white masses previously mentioned; the latter were most numerous near the pyloric orifice. About 9 cm. from the cardiac orifice on the greater curvature, and 3 cm. posterior to the attachment of the gastro-colic omentum on the posterior wall of the stomach, were two openings, both communicating with the cavity above mentioned. The larger and posterior was 9 cm. in diameter; the smaller, anterior, 2 mm. in diameter. The gastric mucosa excepting for these openings was normal and of the usual pale pink color with practically no evidence of blood staining. The edges of the ulceration as seen from within the stomach were smooth and fairly regular in outline. There was no evidence of thickening. The opening into the stomach was now continued into the duodenum along its right side. About 3 mm. below the pylorus on the left side of the duodenum, adjoining the pancreas was another large irregular opening, 1.5 cm. in diameter; the edges were smooth, the outline showing a few indentations. This communicated directly with the cavity previously mentioned. On continuing the opening into the duodenum a second opening was found just internal to the papilla of Vater, about 2 cm. in diameter. This resembled the first opening described in the duodenum in possessing smooth edges and an irregular outline and in communicating with the cavity above described.

The *gall bladder* was opened and found to contain nine small, angular, facetted, reddish-colored gall stones, the largest measuring 5 mm. in diameter. The *cystic duct* contained no gall stones and was patent. The *common bile duct* was patent and contained no stones. Its opening was situated just externally to and to the right of the second opening into the duodenum. The duct of Wirsung could not be found in the papilla, but on carefully passing a probe through the common duct, at the base of the perforation just internal to the papilla it could, by slightly altering its course, be passed through the papilla. The duct of Santorini could not be found.

On making a section through the head of the pancreas, a portion of normal pancreatic tissue corresponding to the head and measuring 1.5 cm. in transverse thickness and 3 cm. in antero-posterior diameter, could be distinctly seen. The left part of this normal tissue with the duodenum formed the right of the cavity which was bounded above by the stomach and passed outward between the stomach and the spleen, extending upwards to the left from a point about 4 cm. to the left of the middle line. Another arm passed below and behind the spleen and occupied the region of the tail and the left part of the body of the pancreas. The main cavity lay between the colon and stomach and occupied the position of the body and greater part of the head of the pancreas. The inferior boundary was formed by the folds of the slightly developed transverse meso-colon. The whole cavity contained the substance previously mentioned. There was a marked fæcal odor. No trace of normal pancreatic tissue was found with the exception of the small portion of the head previously mentioned. The source of the hæmorrhages was from the splenic artery as far as could be observed in the short time allowed for the examination.

Examination of the pancreas with the exception of the portion of the head previously described showed that it was replaced by masses of firm, whitish, friable, opaque material with a fæcal odor. Some semblance of the alveolar structure of the pancreas could be made out in places. This was mixed with recent blood clot, semi-fluid and apparently only a few hours old, suggesting that the hæmorrhage was a secondary and probably terminal event. The dissection of the head of the pancreas showed that the common bile duct and the duct of Wirsung united at least 1 cm. below the orifice of the papilla of Vater.

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Since the renewal of interest in diseases of the pancreas which followed, especially, the notable work of Fitz [3] we have gained much knowledge concerning the nature, frequency, and symptoms of acute pancreatitis.

The experimental observations of Hildebrand,[4] Koerte,[5] Dettmer,[6] Hlava,[7] Williams,[8] Flexner,[9] and others, demonstrated that acute pancreatitis might be produced by various mechanical and chemical injuries to the organ.

The direct relation between the escape of pancreatic juice into the surrounding tissues and the development of disseminated fat necrosis, first suggested by Langerhans,[10] may be regarded as proven since the demonstration of a fat-splitting ferment in the necrotic foci by Flexner,[11] and the investigations of Opie.[12]

The notable observations of Halsted [13] and Opie [14] would seem to indicate that one of the most important causes of acute pancreatitis is the retrojection of bile into the pan-

[3] Boston M. & S. J., 1889, CXX, 181, 205, 229.
[4] Centralbl. f. Chir., 1895, XXII, 297.
[5] Berliner Klinik, 1896, No. 102.
[6] Inaug. Diss., Goettingen, 1895.
[7] Bulletin international de l'académie des sciences de Bohême, 1897.
[8] Boston M. & S. J., 1897, CXXXVI, 345.
[9] Johns Hopkins Hosp. Rep., Balto., 1900, IX, 743.
[10] Arch. f. path. Anat. (etc.), Berl. 1890, CXXII, 252, and Festschr. Rudolf Virchow, 80, Berlin, 1891.
[11] J. Exper. M., N. Y., 1897, II, 413.
[12] Contributions to the Science of Medicine, dedicated to William H. Welch, Johns Hopkins Hosp. Rep., 1900, IX, 859.
[13] Johns Hopkins Hosp. Bull., Balto., 1901, XII, 179.
[14] Johns Hopkins Hosp. Bull., Balto., 1901, XII, 182; also Am. J. Med. Sc., 1901, CXXI, 27.

creatic duct, such as may occur in connection with the passage of a stone or its lodgment in the diverticulum of Vater, in cases where the opening of the duct of Wirsung occurs at a point sufficiently far from the outlet of the common duct to admit of its patency at the time of obstruction of the latter. Repeated experiments have shown the possibility of producing pancreatitis in this manner. Apart from Opie's and Halsted's observations a study of the literature reveals the striking frequency of the sequence of acute pancreatitis upon cholelithiasis. In my first case of pancreatitis the onset of an acute hæmorrhagic inflammation followed immediately the passage of a stone which was found, at necropsy, in the common duct.[15]

Peiser[16] has recently called attention to a suggestive relation between acute pancreatitis and parturition. Eight out of 121 cases collected by him occurred during the puerperium. He accordingly suggests that the changes which give rise to this process may be similar to those occurring in the liver and other organs in eclampsia, and due possibly to like toxic substances. Münzer,[17] on the other hand, calls attention to the possibility that the primary necrosis may follow embolism of small vessels in the pancreas with giant cells from the placenta.

Those cases of acute pancreatitis which go on to suppuration, the "subacute" form of Robson and Moynihan, have especial interest in that they alone are amenable to surgical treatment. In most of these cases the onset is as acute as in the hæmorrhagic form, but the symptoms are, as a rule, less aggravated and the changes are not at first of sufficient extent and gravity to cause the death of the patient. Subsequently the necrosis and secondary infections result in the formation of more or less extensive abscesses with the characteristic contents, in which may lie larger or smaller portions of the sequestrated necrotic pancreas. In view of the satisfactory results of prompt surgical interference, the question of early diagnosis in these cases is extremely important. As has been said the symptoms are more or less characteristic. The onset, sometimes ushered in by an attack of biliary colic, is usually characterized by sudden, intense, abdominal pain, localized, as a rule, in the epigastrium but often more or less general and associated with obstinate vomiting and collapse. The fever is not, as a rule, excessive. In some instances the attack may be followed by or associated with jaundice. In the course of a few days the acute symptoms subside, but there remains epigastric tenderness with fever, possibly chills, sweating and evidence of deep abscess. Vomiting is often obstinate. Not infrequently a deep mass may be felt. This mass, as is strikingly emphasized by our cases, may extend on either side into regions considerably distant from the normal limits of the pancreas. It may occupy a situation such as to suggest a paracholecystitis (Case IV) or a paranephritic abscess (Case I). It may be confounded with the results of perforation of the stomach, intestine, or gall-bladder. The cases reported emphasize, especially, this variability in the position of the tumor mass; in two, the tumor extended to the right of the median line; in one, to the left; in two, it lay about in the median line. A deeply-seated inflammatory mass in the upper abdomen, when perforation of the stomach, intestine, or gall-bladder is improbable, should always suggest a suppurative pancreatitis, especially if the onset has followed shortly after attacks of biliary colic.

In cases of this nature careful study of the excreta may be of a certain help. The gross observation of fatty stools is not of very great clinical importance, although Ury and Alexander[18] assert that a discharge of large quantities of liquid fat after the passage of solid, formed fæces is almost diagnostic of extensive pancreatic affection. The determination of the relation of neutral fat in the stools to the fatty acids and soaps may be of assistance. In extensive pancreatic disease there is an interference with the normal fat splitting in the intestine—amounting, ordinarily, to from 70 to 80 per cent of the fat. Before passing judgment upon either of these questions it is, of course, important that the patient should be subjected to careful experimental feeding. According to Ury and Alexander there are three possibilities with regard to abnormalities in the fat content of the fæces in pancreatic disease:

(1) There may be an increased quantity of fat with a diminished fat splitting.

(2) There may be an increased quantity of fat with normal fat splitting.

(3) There may be a normal quantity of fat with diminished fat splitting.

Unfortunately, the careful feeding necessary for thoroughly satisfactory observations of this sort, is usually impossible in acute pancreatitis.

Interference with the digestion of fat is often associated with deficiency in the proteid digestion. The mere discovery of muscle fibres cannot, however, be regarded as an abnormality, and, apart from the quantity of meat taken, it may depend upon various other conditions disturbing the movements, secretion, and absorptive powers of the small intestine. Oser[19] lays some stress upon the importance of the evacuation of quantities of solid fæces which are unduly large relatively to the diet taken.

Glycosuria is rare and of little diagnostic importance. One would expect it to follow only most extensive pancreatic destruction; we know nothing of any selective influence of acute inflammatory processes in the islands of Langerhans.

A test which may prove of considerable importance, is that suggested by Opie who, in one case of acute hæmorrhagic pan-

[15] Boston M. & S. J., 1889, CXXI, 506.

[16] Deutsche Zeitschr. f. Chir. LXV, quoted by Münzer, Centralbl. f. d. Grenzgeb. d. Med. u. Chir., Jena, 1903, VI, 490, 529, 573, 619, 664.

[17] Münzer, Centralbl. f. d. Grenzgeb. d. Med. u. Chir., Jena, 1903, VI, 490, 529, 573, 619, 664.

[18] Deutsche med. Wchnschr., 1904, XXX, 1311, 1345.

[19] Die pathognostischen Symptome der Pancreaserkrankungen, Die deutsche Klinik, etc., Berlin, 1901, 151.

creatitis was able to demonstrate the probable presence of a fat-splitting ferment in the urine; Opie[20] pointed out that there was a reasonable possibility that in acute pancreatitis traces of lipase might be demonstrable.

The recent observations of Hewlett[21] upon this question are of considerable importance. This observer has determined that lipase appears in the urine after a variety of insults to the pancreas of dogs; it is found in greatest amount as a result of experimental acute hæmorrhagic pancreatitis. The procedure adopted by Hewlett for determining lipase in the urine is a modification of the Kastle-Loevenhart method depending upon the hydrolytic cleavage of ethyl butyrate in a solution containing lipase, into butyric acid and alcohol. The urine is then extracted with ether and the amount of butyric acid determined by titration. The following is the method in detail: "Five cubic centimeters of urine are placed in each of three flasks. The urine in the second flask is then boiled. To the urine in the third flask are added three drops of a one per cent solution of phenolphthalein and N/10 sodium hydrate solution is allowed to run in from a burette until a faint pink color appears. The amount of sodium hydrate solution used is read off and a like amount is added to the first and second flasks. To each of these two flasks, the first of unboiled urine, the second of boiled urine, is then added twenty-five hundredths cubic centimeter of ethyl butyrate and one-tenth cubic centimeter toluene, and they are placed in a thermostat at 39° C. for about twenty hours. The toluene is added in order to prevent the growth of bacteria. At the end of this time each flask is taken out and sufficient N/10 hydrochloric acid is added to more than neutralize the alkali previously added by five-tenths cubic centimeter. Each specimen is then shaken in a separating funnel with fifty cubic centimeters of redistilled ether, and the ether is separated. After adding three drops of a one per cent solution of phenolphthalein to twenty-five cubic centimeters of pure alcohol, the latter is brought to the neutral point. The ether extract from the separating funnel is now added to the neutralized alcohol and its acidity is determined by titrating with N/20 potassium hydrate solution. Any decided difference between the acidity of the ethereal extracts of the boiled and of the unboiled urine is due to the butyric acid formed by the cleavage of the ethyl butyrate; and where the difference in acidity is at all great the odor of this butyric acid can be easily recognized."

It is greatly to be regretted that this test was not made in the first case. Directions had been left to carry it out which were interfered with by an unfortunate accident.

It is an interesting fact that in three of these cases the presence of gall stones was proven. In two they were found at autopsy. In a third, our last case, the gall bladder was not explored but repeated attacks of characteristic biliary colic had occurred, one at the onset of the pancreatic symptoms. In the other two instances the gall bladder was not examined although in Case IV the history was decidedly suggestive of cholelithiasis.

Consideration of these cases also tends to impress one with the feeling that pancreatic disease ought to be more commonly recognized than is the case. The complex of symptoms is, in many instances, characteristic. In all of these cases a diagnosis was made. In the four cases which fell under our observation a positive diagnosis was made in two instances, and in one, pancreatitis was suggested as the strongest possibility. In Case IV the correct diagnosis was made by Professor Halsted. In Case III, which I did not see, Dr. Bloodgood recognized the condition.

The most important point brought out by the review of these cases seems to me to be the favorable result of early operation. Of the four instances of suppurative pancreatitis which were operated upon, three recovered. In Case II, in which there was a fatal result, the patient had been in a miserable condition for three weeks before operation.

The fourth instance was clearly a case of gangrenous pancreatitis.

Final considerations:

(1) A consideration of these five cases would seem, in the first place, to emphasize the importance of the relation between cholelithiasis and pancreatitis.

(2) It should further call attention to the importance of an early diagnosis. Relief can be expected only from early operation and drainage, and while it may be truly said that a positive diagnosis is often difficult, yet there are few conditions with which suppurative pancreatitis is likely to be confounded, in which exploration is not the proper and conservative course.

[20] Johns Hopkins Hosp. Bull., 1902, XIII, 117.

[21] J. Med. Research, Bost., 1904, XI, n. s. VI, 377.

DIAPHRAGMATIC GROOVES ON THE LIVER.

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Introduction.

Grooves on the convex surface of the liver have been more or less carefully observed and studied since the close of the 16th century. Early in the 17th century Fernel (1602) and, sixty years later, Glisson (1666) described them and offered explanations for their existence, designated by Cruveilhier (1874) as "*opinions singulières.*" In the middle of the next century, Morgagni (1761) described some grooves found on the liver at the autopsy of an old woman, and about one hun-

dred years later Cruveilhier (1856) first distinguished the two kinds of grooves now designated costal and diaphragmatic.

Costal grooves occur most frequently on the lateral surface of the right lobe, extending sometimes upon the anterior surface. According to some authors they are impressions caused during life by compression or constriction of the thorax or abdomen due to tight clothing or to chronic pulmonary lesions. They are single or multiple, broad and superficial, rarely narrow and deep, their direction corresponding to that of the ribs which made them. Soulé (1902) describes three varieties: (1) very faint impressions that disappear after the liver has been removed from the body for a certain time; (2) simple grooves deeper than impressions forming a definite, permanent groove covered by normal peritoneum; (3) cicatricial grooves which may be shallow or deep, temporary or permanent. The distinguishing characteristic is the replacement of the peritoneum lining the grooves by cicatricial tissue, which is permanent even though all other signs of the groove disappear.

In bodies autopsied soon after death these grooves, according to Leue, are found most frequently in women. A systematic examination of 516 bodies autopsied at Kiel showed such grooves to be present in 56 per cent of the females and in only 5 per cent of the males. In this laboratory where most of the subjects are male, costal grooves, usually multiple, have been found in a large percentage of the cases. Since dissecting material is not available for embalming until 48 or more hours after death, these grooves may be due to post-mortem pressure of the liver against the ribs with the body supine.

Diaphragmatic grooves, single or multiple, occur most often on the ventral and superior surfaces of the right lobe of the liver and on the ventro-lateral border. They may also exist on the lateral or dorsal aspects of this lobe and rarely on the ventral surface of the left lobe. In a large percentage of cases they are approximately parallel with the falciform ligament and with one another and so far as observed here are always at an angle with the direction of the ribs. In form they vary from mere slits to furrows 7 millimeters wide at the bottom, in length from 1.5 to 11 centimeters and in depth from impressions of less than 1 to sulci of 18 millimeters. Their sides may be parallel or widely diverging, rarely slightly converging. They may or may not contain folds of the diaphragm.

Besides these grooves which have no apparent phylogenetic or ontogenetic significance, Thomson (1899), Rathcke (1896) and others have described and figured narrow fissures commonly present on the Spigelian and quadrate lobes and on the inferior surface of the right lobe. These are held to be persistent embryonic characters, corresponding to fissures more or less distinct in the adult anthropoids and lower forms.

Since Cruveilhier's (1856) recognition of two classes of grooves, the diaphragmatic have been studied by French, German, and Italian investigators who have offered various theories to account for their occurrence. Turner (1898) in England has paid some attention to these grooves but no contributions to the subject have been published by American anatomists. Except brief references in Quain's Anatomy (1898) and in some text-books on pathology, there is no literature on this subject in the English language. It is therefore intended to give a brief résumé of work already recorded, together with results obtained in this laboratory.

History.

That these grooves are of common occurrence, that they exist most frequently on the convex surface of the right lobe of the liver, that they are usually multiple and nearly parallel with the falciform ligament, seems to be the consensus of opinion. But in regard to the sex in which they are most often found, to their presence in youth and infancy, to their association with certain pathological conditions, to their relations with the diaphragm and to their cause, widely differing opinions are expressed.

Concerning the frequency of these grooves there is great scarcity of adequate information, Mattei (1890) alone having kept a record of the total number of bodies examined. He found sixty-nine grooved livers out of one hundred and forty-six cases, about 41 per cent. Other authors have recorded only the sex of the individual and the total number of grooved livers found.

The sex in which these grooves most commonly occur has been the subject of much discussion. Turner (1898), Zahn (1882), and Jacquemet (1896) claim they are found more frequently in men; Charpy (1901) asserts them to be rare in men but common in women. The fifty-eight cases reported by Séglas were all female. The autopsies, however, were made at the Salpêtrière, a home for aged women. Cruveilhier (1874), who also noticed the grooves in a large number of bodies at the same institution, does not express an opinion as to their frequency in men. Buy (1904), who found these grooves in twenty-nine women and twenty men, also claims that they occur much more commonly in women, but he takes no account of the sex or number of bodies in which grooves were not found. In a systematic examination of 146 cadavers, 87 male, 59 female, Mattei (1890) found grooved livers in 26 men and 35 women.

Excluding Séglas' (1902) fifty-eight cases which can have no bearing on relative frequency in the two sexes, the following table gives the number and sex of all cases of which record has been found:

TABLE I.

	Male.	Female.	Unknown.
Mattei	26	35	0
Buy	20	29	3
Kerr[1]	14	1	3
Jacquemet	7	1	0
Tigri	3	0	0
Guéniot	0	2	0
Caryophyllis	1	0	0
Michaut	1	0	0
Jackson[2]	1	0	0
Bagaloglu	0	1	0
Meckel	0	0	1
	73	69	7

The age at which these grooves may appear is another disputed point. Jacquemet (1896) claims that they are found only in subjects over fifty years of age, at the same time recording a case of forty-eight years. Charpy (1901) says they do not exist before the fifteenth year and are most frequent in old age. Buy agrees with him and lays special stress on the fact that they are never found in infants. On the contrary, Mattei (1890) believes that they may be found at all ages and even during intra-uterine life, but gives no account of finding them in the youth, infant or fœtus. Orth (1888), however, reports the occurrence of most beautiful sagittal furrows on the liver of a child which, born prematurely at seven months, died soon after birth.

Data upon the location of these grooves are more satisfactory. Buy (1904) finds them most often on the highest part of the superior surface of the right lobe sometimes extending upon the dorsal surface, but never reaching to the ventro-inferior border, although they occasionally reach to the center of the diaphragm, or even to the right wall of the vena cava. He also finds them on the left lobe, usually fine and faintly marked. In one case, however, the groove on the left lobe was more distinct than those on the right. Meckel (1812) reports a similar condition, where there were six well-marked grooves on the left lobe and three on the right; while Mattei (1890) finds them sixty-six times on the right lobe and four times on the left.

The record of the number of grooves is also complete and shows them to be usually multiple. They are said to vary from 1 to 9, Jacquemet (1896) claiming that their occurrence singly is rare, while Soulé (1902) makes their multiplicity an important distinction between them and costal grooves. Buy (1904) observes them occurring most frequently in twos and threes.

The direction of these grooves is described as "antero-posterior," "extending from the thick to the thin border of the liver," "lying in the long axis of the body," "longitudinal" and "parallel with the falciform ligament." According to Buy (1904), their direction is antero-posterior, they are parallel in the middle, converging dorsally and diverging ventrally. Rarely the converse is true. They are often curvilinear, the concavities looking toward the falciform ligament when placed laterally, away from it when placed near the ligament, or occasionally toward each other thus (). In one case he found a groove shaped like an italic letter *S* and in another one like the letter Y.

The form as given by different authors is deep and narrow or shallow and broad, with varying proportions. The length is said by Buy (1904) to be usually from 5 to 6 centimeters, with a minimum of 2 and a maximum of 9. He also says they habitually increase in length toward the median line. Jacquemet's (1896) limits are from 3 to 10 centimeters, the grooves increasing in length from right to left or from left to right. Caryophyllis (1889) found four grooves ranging in length from 10 to 12 centimeters; thus an extreme variation from 2 to 12 centimeters is reported. Most writers describe the grooves as narrow, but Buy (1904) claims that their breadth is relative to their form and indicates two classes, the one gutter-like with a width of from 5 to 12 millimeters, the other, which he designates as true grooves, are narrow, only a few millimeters in breadth. There is also much variation in depth. Mattei (1890) finds some sulci so shallow as to be seen only on the most careful inspection, others 15 millimeters deep. Jacquemet's (1896) series ranges from 2 to 11 millimeters and Michaut (1888) records a case of 25 millimeters, while Buy (1904) gives as his limits less than 1 centimeter to 2.3 centimeters. He holds that the grooves may increase in depth from the median line laterad or the reverse or the deepest grooves may lie in the middle of the series, flanked by shallower grooves, the first arrangement being the most frequent. Moreover the deepest is usually the longest and the depth increases with the age of the subject, a fact also noted by Mattei (1890).

Much stress is laid on the condition of the diaphragm and its relation to these grooves. Observations and opinions on the former may be placed in one of two general classes: first, the diaphragm overlying a grooved liver always has folds or hypertrophied digitations or fascicles of the musculature; to this the majority of authors agree. Second, that such a folding or hypertrophy may or may not exist, a view held by only three authors, Buy (1904), Guéniot (1898), and Bagaloglu (1899).

Charpy (1901), Caryophyllis (1889), Cruveilhier (1874), and Tigri (1873), believing folds or digitations to be always present, record no observations as to other conditions of the diaphragm. Zahn (1882) agreeing with these authors claims that the hypertrophied digitations of the diaphragm have their origin at its costal insertions and may degenerate, leaving only the two serous layers and some connective tissue. Séglas (1886) finds the diaphragm sometimes adherent to the liver and observes stripes of degenerated muscle fibers in the diaphragmatic musculature so placed as to have no definite relation to the grooves in the liver. An entirely different condition is described by Mattei (1890), who believes that

[1] Recorded in this paper.

[2] Not published but record given to me by Dr. Jackson, of University of Missouri.

there is a congenital unequal distribution of the musculature of the diaphragm, resulting in thickened muscle bundles alternating with thinned areas.

Of the second group Buy (1904) alone discusses in detail the condition of the diaphragm. He finds three possibilities: first, it is unmodified and passes over the grooves like a bridge; second, still bridging the grooves, it is uniformly thickened; third, it sinks more or less deeply into the grooves, is thin and transparent over the intermediate mounds of liver and is thickened at the bottom of the grooves. This he believes due to functional hypertrophy and a sliding downward of the muscle fibers from the sides, so that sometimes there is no muscular tissue at the neck of the groove. The mounds of liver between the sulci cause a stretching and consequent thinning of the overlying musculature.

Connected very closely with the condition of the diaphragm is its relation to the grooves. Charpy (1901) states that an examination of the liver and diaphragm in situ shows that the folds exactly fill the grooves and with this Tigri (1873), Mattei (1890), and Séglas (1886) agree. On the contrary Buy (1904) finds, as already mentioned, that the diaphragm may bridge the grooves or may fill them completely or in part. Agreeing in the main with Charpy (1901), Zahn (1882) admits that sometimes the fold only partly fills the groove, when the depth is great.

Another point of interest is the condition of the peritoneum and parenchyma at the bottom of the grooves. That both are normal is held by Charpy (1901), Orth (1888), Séglas (1886), Jacquemet (1896), and Guéniot (1898). Buy (1904) and Mattei (1890) agree that the peritoneum is unaltered but do not mention the parenchyma. The former adds that peritoneal adhesions never occur at the bottom but on the sides of the grooves or on the projecting liver surface. As opposed to this Liebermeister (1864) and Klebs (1868) find alterations in both, the peritoneum having become thickened and the parenchyma having degenerated and atrophied.

The pathological conditions associated with these grooves according to some authors are many, while others have made no record of their co-existence. Charpy (1901) states that the liver is bomb-shaped, its vertical diameter is increased, and the inferior edge, extending beyond the costal margin, approaches the iliac crest. The gall bladder is pinched laterally and projects downward, the Spigelian lobe becoming pediculated, thin and elongated. The inferior part of the right lobe becomes separated, forming the lobe of Riedel. Some portions of the left lobe atrophy and are transformed into membranous appendices which fold in every direction. There are also found on the same subjects external malformations of the thorax and in the abdomen, bilocular stomach and movable kidney. In general Buy (1904) agrees with these observations but emphasizes the constant co-existence of signs of habitual compression of the thorax, the liver and other abdominal viscera. He enumerates as these signs, deformed costal skeleton, contraction of the transverse diameter of the chest, decreasing of the xiphoid angle, changes in the liver described by Charpy (1901), which, together with costal grooves, characterize the "liver of constriction," costal grooves on the spleen, enteroptosis and nephroptosis. A different group of co-existent pathological conditions is given by Liebermeister (1864), whose observations were confirmed by Zahn (1882), Klebs (1868), Jacquemet (1896), and Séglas (1886). These authors found in most cases that the grooves were associated with diseases of the lungs and pleura, resulting in difficult respiration; double goitre compressing the trachea was also noted by Zahn (1882). Séglas (1896) examined the records of autopsies held at La Salpêtrière for a period of five years and found fifty-eight cases of grooved livers, in only five of which the lungs were sound. In the remaining fifty-three cases, pleurisy was present in twenty-four, hydrothorax one, pulmonary congestion twenty-four, pneumonia twenty-two, broncho-pneumonia eight, chronic bronchitis four, emphysema three, tuberculosis two. These lesions were combined in a different manner in thirty-six cases. In six of the remaining seventeen, both lungs were involved: one had hydrothorax; two, pulmonary congestion; three, broncho-pneumonia. On the right side alone acute and chronic pneumonia were present in four cases and broncho-pneumonia in one. On the left side alone, pneumonia was found four times, pulmonary congestion once, pleurisy with thickening and adhesions once. The pathological conditions found by Tigri (1873) and Mattei (1890) concern the diaphragm and have been enumerated in the consideration of that structure.

Causes.

The desire to account for these grooves has led to much discussion and to the development of several distinct theories which may be placed in one of three classes. The oldest hypothesis, that of constriction by clothing, is suggested by Morgagni (1761), who, in reporting his one case, an old woman, remarks that if such grooves were found only in women, there might be some ground to suspect a causal relation in the pressure exerted by the corset. This view is more positively stated by Cruveilhier (1874) who, finding these sulci in a large number of old women at the Salpêtrière, concludes that constriction by the corset causes folds in the diaphragm, these in turn creasing the liver. Charpy, a strong advocate of this "constriction" theory, has in a letter to me extended its application to grooved livers in men, claiming that tightly drawn belts would force the livers upward into the narrower part of the diaphragmatic dome thus subjecting them to increased lateral pressure. After a careful study of this problem in Charpy's laboratory, Buy (1904) accepts the constriction theory and vigorously defends it, giving the following reasons: the much greater frequency of grooves in women; the constant co-existence of signs of habitual external thoracic compression; the presence of these grooves on the constriction type of liver; concomitant deformities of abdominal viscera; complete absence of such grooves in infants and increased frequency with advancing years. He

asserts that they are due neither to a congenital condition nor to a teratological disposition of the diaphragm, nor to its irregular contraction dependent upon difficult respiration. Two types of the grooved "constriction livers" are recognized, masculine and feminine, the former caused by "low constriction" as of a belt, the latter by "high constriction" as of a corset. The superior surface of the masculine type is characterized by the presence of a marked bomb, bearing one or more grooves of varying depth. This form he attributes to the crowding of the liver upward when the dimensions of the abdominal cavity are decreased, thus causing a heaping and consequent folding of the liver substance sometimes accompanied by, or resulting in, a corresponding fold of the diaphragm. Two varieties of the feminine type are described; the one liver is flat and relatively slightly deformed, often anteverted, marked by shallow, oblique, diverging grooves situated only on the cephalic surface; the level of greatest pressure in these cases is high. The other liver, compressed transversely, much deformed, is the type of "constriction liver," costal impressions are distinct, the right lobe is high, thick, bomb-shaped, grooved longitudinally, elongated, often crossed near its caudal border by a transverse groove, separating what is known as a "lobe of constriction." The pressure in this type is at a lower level than in the preceding, but in both cases the lower part of the thorax is narrowed, resulting in a consequent folding and grooving of the plastic liver. The masculine and feminine types are not, however, restricted to the male and female sexes respectively; the former frequently occurs in women and the latter occasionally in men. Bagaloglu (1899) accepts the constriction theory, as does Guéniot (1898) for those cases in which there are no corresponding diaphragmatic folds.

Broadly speaking the next hypothesis also involves constriction, but with this difference, that the pressure is due, not to external artificial causes but to internal pathological conditions. Dyspnea, resulting from difficult expiration, is held by Liebermeister to be the fundamental cause of these sulci, which he calls expiratory grooves. He asserts they are never formed by the diaphragm but are due to the pressure of the caudal borders of the ribs, which are drawn in by the exaggerated action of the external oblique and transverse abdominal muscle during forced expiration. This muscular action is often reinforced by the permanent depression of the diaphragm commonly accompanying difficult expiration, and limiting the upward movement of the liver. This action must be long continued to produce permanent grooves. To this interpretation Klebs (1868) agrees, but believes that scoliosis, rachitis, and pressure of corsets may also narrow the thorax transversely and thus cause such grooves. Zahn (1882) says he is in accord with Liebermeister (1864) in the belief that the grooves result from long continued difficult respiration but differs fundamentally as to the mechanism of the process. The primary cause is impeded *inspiration*, to compensate for which a gradual hypertrophy of certain portions of the diaphragm takes place. This thickening begins at its costal insertions and gradually extends centrally, so that even before grooves have appeared on the liver, such a diaphragm viewed by transmitted light shows the existence of thickened fascicles separated by thinner areas. Ultimately these thickened digitations by downward pressure during the contraction of the diaphragm cause grooves on the liver. This author is not convinced that the corset can primarily form sulci but it may increase the depth of those already existing. Séglas (1886), Michaut (1888), and Jacquemet (1896) all accept this view with slight modifications.

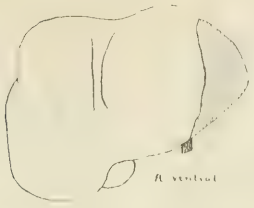
The two remaining theories are held by those who believe the primary cause to be a congenital condition of the diaphragm. Mattei (1890) claims that there exist in the diaphragm even before birth alternate thin and thick areas, the musculature sometimes being entirely absent in the thin parts; that since the growth of the liver is greatest along the lines of least resistance, the parenchyma pushes up beneath the thin areas with the result that grooves and elevations alternate on the surface of the organ. He denies the action of any other cause, admitting only that grooves may be deepened by the physiological contraction of the thickened muscle bands lying in them. The other theory advanced by Tigri (1873) differs fundamentally from the preceding. He maintains that the sulci are due to the presence of teratological, cylindrical, muscular reliefs on the caudal surface of the diaphragm, which by constant close contact impress the liver surface with corresponding grooves. He associates these reliefs with other abnormal muscular conditions of the diaphragm. He also denies the action of any other cause. Orth (1888) must likewise be classed with those who believe that the grooves may be congenital, basing his belief on the fact that the capsule and parenchyma at the bottom of the grooves remain unaltered; at the same time he is unwilling to deny the claims of Zahn (1862) and Liebermeister (1864).

Material.

To the foregoing history it is now possible to add the record of 17 cases found in this laboratory and 16 from the museum of Cornell University kindly loaned by Dr. Kerr. Of the 17 cases, 5 were from adult and 2 from fœtal subjects. In accordance with the law, bodies cannot be delivered to this department until at least 48 hours after death. Thus in all subjects received here post-mortem changes have taken place before embalming. The preserving fluid used in 11 of the adults was the carbolic mixture[3] advocated by Mall (1896), in 2 an arsenic-formalin combination; the history of the remaining 2 is wanting. After the injection of 6 quarts of the carbolic mixture under constant pressure, some of the bodies were placed in tanks over wood alcohol and in a few months were transferred to vats containing 3 per cent of carbolic acid; others were put directly into the vats. With the exception of subject 201, which lay on the right side, all subjects are embalmed in the supine position and in

[3] Carbolic acid one part, alcohol two parts, glycerine two parts.





















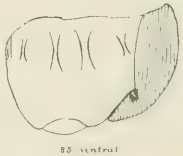


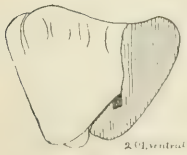
















the tanks have that position best suited to advantageous use of the space. Of the adult subjects received here about 79 per cent are old males, 7 per cent old females, 13 per cent young males, 1 per cent young females. The fœtal material is preserved either in alcohol or formalin; the 2 subjects in which grooved livers were found, were in alcohol.

The great variety of size and form found among these livers as shown on page 369 made it convenient to group them for description according to the number of grooves present; also for convenience the sulci are numbered from right to left.

Livers with One Groove.

Of these there were six, five adult, one fœtal; three male, one female, two unknown. They differ widely as to form, weight, size, and character of the sulcus. Of the entire series X approaches most nearly to the form and size of the His model, the differences between them being no greater than may exist between any two normal livers. It is not bomb-shaped nor deformed in any other way, its only peculiarity being a moderately deep, curved, slit-like furrow on its ventral surface.

In extreme contrast to this is A, which shows a condition usually considered uncommon but present to some degree in 9 of these cases; this liver lying almost wholly in the right hypochondrium, has an unusually broad lateral surface and the so-called dorsal surface looks mesad. The organ is much enlarged and the right lobe elongated; it is marked by two faint costal impressions and on the lateral surface by a long, wide, moderately deep, diaphragmatic sulcus extending vertically. A marked bomb projects upward and forward, bounded laterally by the sulcus.

Subject 89, a liver of moderate size having the right lobe much elongated, the Spigelian lobe and gall-bladder both pinched and elongated, also lies mainly in the right hypochondrium. It is so flattened that the dorsal and inferior surfaces lie in one plane, which looks mesad. There are three costal impressions and on the lateral surface one faint sulcus which is broad and very shallow. There is a strong resemblance between 89 and 104, the next to be described. This too is narrowed transversely and lies chiefly in the right hypochondrium, its much elongated right lobe extending into the right lateral abdominal region; the gall bladder is elongated but the Spigelian lobe is normal in form. The dorsal and inferior surfaces lie in the same plane and look mesad. A well-marked bomb projects from the ventro-lateral border, just laterad of which is a wide, rather deep groove; two costal impressions lie dorsad of the groove.

Of moderate size, not elongated, situated entirely in the right hypochondrium, except for the small flattened extremity of the left lobe, 48 is peculiar on account of a distinctly fœtal position of the gall bladder, which lies in a fossa terminating three centimeters from the inferior border of the right lobe. As in the three preceding livers the dorsal and inferior surfaces lie in the same plane and look mesad. A distinct bomb is seen on the ventro-lateral border. On the lateral surface close to the dorsal border, extending upon the superior surface and containing a fold of the diaphragm is a long, deep sulcus, very narrow at the bottom, spreading at the top; costal impressions groove the dorsal border. In this subject, a male of 43 years, the diaphragm is firmly adherent to the liver between the leaves of the coronary ligament and to the chest wall as high as the fifth interspace, a little laterad of the nipple line and as high as the ninth rib in the mid-axillary line; it is also firmly adherent to the base of the right lung. On the superior surface there is no indication of the fold running nearly parallel with the 8th rib so distinctly seen on the ventral surface. The pleural surfaces of the fold are firmly bound together by adhesions which are continuous with a thickened mass of scar tissue covering a large area in its vicinity. Both the musculature in the fold and the underlying peritoneum are distinctly thickened. The lungs are tubercular, the right being firmly adherent to the chest wall and to the diaphragm over a large area surrounding the fold. Another abnormality in this subject was a bilocular stomach. The last of this group, 120, is the liver of an eight months' female fœtus; it appears normal in every way except for a faint, broad, shallow sulcus on the ventral surface near the lateral border.

Livers with Two Grooves.

Of the livers with two grooves 80 is moderate in size, lies chiefly in the right hypochondrium, has a prominent bomb projecting from the ventral and lateral surfaces. This is bounded laterally by a long, wide diaphragmatic groove of considerable depth, reaching from the superior surface to near the inferior margin, and carries on its summit a faint, shallow sulcus. The lungs in this subject, a male 78 years of age, were normal with slight lateral pleuritic adhesions. The inferior surface in this liver is distinct from the dorsal which looks nearly mesad.

From an adult female subject, 103, the liver is of moderate size, somewhat elongated transversely, has two costal impressions and a small bomb directed ventrad. The dorsal and inferior surfaces are in one plane and look dorsad. Of the two diaphragmatic grooves the deeper, shorter and broader, lies on the ventral surface of the right lobe; the other very faint, is on the ventro-lateral border. The lungs showed no indications of disease; the right lung, however, had five lobes and was slightly adherent to the diaphragm.

The next specimen, 115, is most interesting because it is distinctly grooved and occurred in a male fœtus of about 9 months. The liver is in other respects approximately normal except for some post-mortem depressions and curling of the edges. The broader of the two grooves, 1.9 centimeters long, .15 centimeters deep, with widely diverging sides, is placed on the ventro-lateral border and is parallel to the falciform ligament and to the overlying muscular fibers of the diaphragm. The other groove situated a little mesad of the first on the ventral surface is 1.7 centimeters long, shallow, wide and directed obliquely so that the superior extremities

of the two grooves if continued would meet within a short distance. The muscular fibers of the diaphragm lying in this groove are parallel with it. There are no indications of thickened bands or thinned areas in the diaphragm, but a part of its tendon lies in the cephalic end of the longer groove (Fig. 3).

Livers with Three Grooves.

Liver 76 is flattened so that the inferior and dorsal surfaces are in one plane which looks dorso-mesad. It has two faint costal impressions and near the ventro-lateral border a small bomb. The sulci vary widely as to size and form; number one lying on the lateral surface near the dorsal border is short, wide and very shallow. Two, about a centimeter mesad of one, is 8 centimeters long, .5 centimeters wide at the bottom and 1.4 centimeters deep with widely divergent sides. The third, on the summit of the bomb, is 8 centimeters long, 1.8 centimeters deep and very narrow, its almost perpendicular sides making a sharp contrast with those of the other grooves. The great omentum, tucked up between the liver and the diaphragm and adhering to both, filled the two wide grooves and covered the narrow one without dipping into it, excluding the diaphragm from any close relation with the furrows. The pleura of both lungs was more or less adherent to the chest wall but not to the diaphragm (Fig. 4).

Like the preceding, this liver, 105, has its dorsal and inferior surfaces in one plane that looks dorso-mesad. It lies chiefly in the right hypochondrium and has two very faint costal impressions; there is no general enlargement nor projection into a bomb. The first groove situated on the dorsal border is very faint. The second, the most distinct, lies near it on the lateral surface; the third, very broad and shallow, is ventral. They are all parallel with the overlying fibers of the diaphragm which fits into them but has no permanent folds. In the neighborhood of the sulci there were on the diaphragm three thin areas alternating with two bands equal in thickness to the rest of the musculature but appearing thicker. The thorax had been cut in the median line, rendering it impossible to determine whether the thinned areas correspond with the grooves or with the ridges between them.

Enlarged in all its dimensions, 112 has a right lobe extending 3.5 centimeters below the costal border, a slight bomb on the ventro-lateral margin, and the peculiar flattened superior surface mentioned by Liebermeister which forms a right angle with the ventral surface. The Spigelian and quadrate lobes and the gall bladder are not, as customary, parallel with the falciform ligament but lie at an angle of 45 degrees to it. The dorsal and inferior surfaces are in one plane directed dorsad. The extremity of the left lobe is much flattened and elongated so that it overlaps the spleen and is in contact with the left parietes. A very shallow sulcus situated near the dorso-lateral border extends over the superior upon the dorsal surface. Two centimeters mesad is a second, passing over the same surfaces and curving so as to meet the preceding groove on the dorsal surface; its lateral portion is deep with widely diverging walls, its superior shallow, its dorsal slightly deeper. The third sulcus, 1.8 centimeters deep, .7 centimeters wide, parallels the second on the lateral and superior surfaces and has nearly vertical walls. All the sulci lie laterad of the bomb and are depressions below the normal surface of the liver; they are not longitudinal but oblique, their inferior extremities making an acute angle with the long axis of the body. Grooves two and three lodge diaphragmatic folds which exactly fill them. The adjacent pleural surfaces of these folds are firmly united by old adhesions, giving the cylindrical reliefs described by Tigri (1873). A thick layer of organized scar-tissue formed by pleuritic adhesions concealed any sign of the groove on the superior surface. The fold lying in groove three passes obliquely from the 8th to the 11th costal interspaces; number 2 passes from the inferior border of the 9th rib over the 12th, its fibers continuing into the right crus. Owing to the adhesions on the right side between the pleura of the thoracic wall and the diaphragm, the line of insertion of the latter was permanently changed to a higher level, corresponding very closely laterally and ventrally to the outline of the lung in expiration. These folds hardened in situ proved on microscopic examination to be the simple infoldings of the diaphragm and its pleura with a thick overlying mass of scar-tissue. The musculature of the folds was thickened. Tubercular nodules were present in both lungs and the pleura was extensively adherent to the thoracic parietes and diaphragm, especially on the right side and in the region of the folds (Fig. 5).

Livers with Four Grooves.

The first of this group, 119, from a male aged 76, is normal in size and shape except that the inferior and dorsal surfaces lie in one plane looking dorsad. The grooves present two distinct types, the deep slit and the shallow groove, the one with parallel and the other with widely diverging walls. These appear on surfaces which do not rise above the normal level, that is, the sulci are depressions of the liver substance. Groove one, a mere slit 1.5 centimeters long, lies on the lateral near the superior surface; the second of the same length but broader is on the ventro-lateral border, the other two shallow with widely diverging walls are on the ventral surface.

The next, 40, from a male subject 43 years old, is large, the right lobe not elongated, the left extending to the edge of the spleen. There is a bomb of large lateral but slight ventral projection; the grooves, 2 on the lateral and 2 on the ventral surface, are shallow, parallel, slightly converging superiorly, with widely diverging walls. The diaphragm is somewhat adherent to the liver over the right lobe, but has no indication of folds.

Livers with Five Grooves.

A moderate ventral bomb, a somewhat elongated gall bladder, the dorsal and inferior surfaces forming one plane and the presence of grooves, distinguish liver 85 from the normal. Sulci 4 and 5 lie on the bomb, 3 bounds it laterally, 1 and 2

are on the lateral surface, 3 and 4 converge toward the superior surface and are long and deep with steeply sloping sides.

Although the next subject, 201, a male aged 80, was embalmed lying on the right side, the liver is not noticeably different from some of the preceding. The left lobe is elongated, nearly equal to the right in length and is flattened dorso-ventrally. The right, not elongated, with distinct dorsal and inferior surfaces, has 2 costal impressions and a slight lateral bomb on the summit of which is a short groove slit-like at the bottom, wide at the top, containing a permanent fold of the diaphragm which crosses obliquely the 8th and 9th ribs. The other grooves, one dorsal and three ventral, are wide and shallow without permanent folds. Except for slight adhesions of the left lung to a portion of the thoracic wall and to the diaphragm, there are no indications of diseased lungs or pleura. The diaphragm hardened in situ shows on microscopic examination that the fold consists of a thickening of the musculature only, the pleura passing smoothly over the fold. There is no thickening of the diaphragm overlying the shallow grooves, the directions of which correspond to that of the muscular fibers.

Liver with Nine Grooves.

The last adult case, 151, a female 78 years old, presents a number of interesting conditions. The liver which resembles the fœtal type in the nearly equal size of the right and left lobes and in its position in the epigastric and both hypochondriac regions, is unusually short and broad and so flattened that the dorsal and inferior surfaces lie in one plane directed dorsad. It is marked by 9 diaphragmatic grooves, 6 on the right and 3 on the left lobe. The only other liver with 9 sulci, reported by Meckel (1812) had this arrangement reversed. Groove 1, shallow, short and broad, is about 2 centimeters from the right lateral border. Two, similar in size and shape, is about 4 centimeters from the border. Three, a little further mesad, is long, deep, concave toward the falciform ligament, with parallel walls which slope from the opening of the groove dorsad and slightly mesad. This forms the lateral boundary of an oval mass of liver substance 9 centimeters long, 7 centimeters wide, which projects slightly beyond the adjacent surface and bears on its summit two well-defined sulci. The other boundary is groove 6, long, narrow, and concave laterad; its walls are not parallel, the one next to the mass is directed dorso-dextrad and the other is almost parallel with the ventral surface of the liver. The planes of grooves 3 and 6, if prolonged would intersect within a short distance. The left lobe has a large, flat, superior surface separated from the ventral by a distinct angle and a well-marked splenic impression on its dorsal surface. The remaining three grooves are on this lobe. Seven, close to and parallel with the falciform ligament, moderately broad and shallow, is for the greater part of its length on the ventral surface but extends upon the superior, where it curves, sinistrad. Groove 8 lying entirely on the ventral surface about 5 centimeters from 7 is very shallow and is directed obliquely toward the median line. The last of these sulci, about 2.5 centimeters from the left lateral border, parallel to it and the preceding groove, is the most distinct on this lobe and lies on both the superior and ventral surfaces.

The gall bladder contains an oval stone, the axes of which are respectively 4.7 and 3.7 centimeters in length. That part of the ventral surface of the gall bladder extending beyond the inferior border of the liver is firmly adherent to the diaphragm over an area measuring 2.5 x 3.5 centimeters.

In situ the diaphragm shows distinct folds corresponding to grooves 3, 6, 8, and 9, which disappear on its removal from the body. The crests and sides of the folds lying in 3, 6, and 9 are formed by thickened bands of musculature not flanked on either side by thinned areas, thus indicating that the thickening is possibly due in part to hypertrophy, not alone to sliding of the muscle fibers. In the region of 9, the diaphragm is thickened over an area greater than that indicated by the groove. The fold itself is also longer and deeper than the underlying sulcus, which points to the formation of the fold prior to the groove. The folds corresponding to grooves 3 and 6 converge superiorly and terminate independently at the tendon on either side of the vena cava. Superiorly they also converge and unite in the thickened area of adhesion between the gall bladder and the diaphragm. Notwithstanding this unusual convergence at the periphery, the folds are parallel with the musculature. The changed direction of the muscle fibers is due primarily to a cholecystitis resulting in an adhesion of the gall bladder to the diaphragm and subsequent formation of scar-tissue, which by thickening and contraction tends to draw together fibers within the area of its influence. This practically makes a point of insertion of the diaphragm upon the gall bladder and adjacent margin of the liver. The diaphragm overlying the mound bounded by grooves 3 and 6 shows by transmitted light alternate thick and thin areas; the former, rather wide bands lie in grooves 4 and 5, the latter correspond to the eminences between these four sulci. The thinning suggests that the thickening is due in part to the migration of intervening fibers, not alone to hypertrophy. There is no modification of the region of the diaphragm in relation to 1 and 2. There are no tubercular nodules in the lungs and the only indications of pleurisy are slight adhesions near the apex of the right lung; but a localized peritonitis in the right hypochondrium has resulted in adhesions between the right lobe of the liver and the diaphragm in addition to the strong adhesion already mentioned (Fig. 6).

One other liver is of interest because it has a suggestive appearance early in fœtal life. Taken from a fœtus of three and a half months, this liver, normal in other respects, has on its ventro-lateral border a slight bomb, limited mesad by a broad shallow groove; while on the superior and lateral surfaces is a series of linear impressions which correspond to alternate thick and thin longitudinal bands in the diaphragm.

Through the kindness of Dr. Kerr of Cornell University,

it is possible to report on 16 additional grooved livers (page 373). The source, preparation, age, and sex of the bodies from which these came are much the same as that of material used in this laboratory. These livers like those already described show a great variety of form and of grooves. Six of them are small, about the size of the His model, four medium, six large, but none are much enlarged. Six of these, 37 per cent, have only one groove. This coincides with the conditions existing in the first series and indicates that single grooves are not so rare as claimed by some authors.

tween a localized peritonitis and the grooves similar to that found in 151.

General Summary.

From the foregoing descriptions and accompanying figures (page 369) it can be seen that grooves occur on livers varying much in form. Some resemble the His model, others belong to one of Charpy's extreme types, the flat, in which the dorsal and inferior surfaces are in one plane; the bomb or dome-shaped which he considers pathological. They vary in size

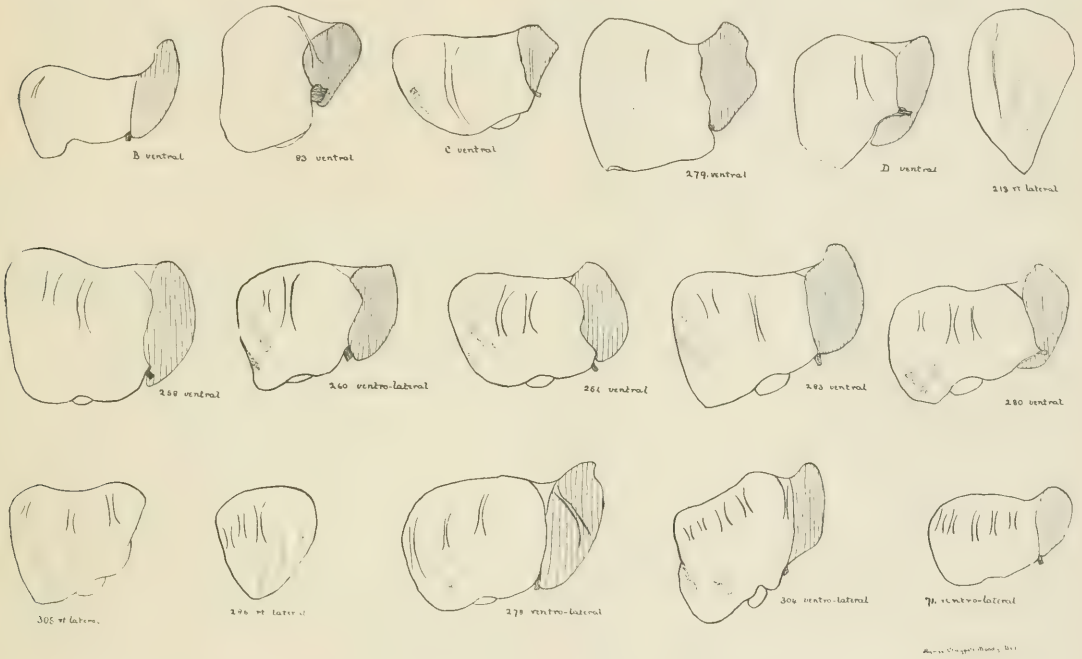


Table 2 gives most of the facts of interest concerning these livers but numbers 83, 278, 71, and 254 show some features that should be especially mentioned. Number 83 is unique in that its single diaphragmatic groove passes from the right lobe to the left across the falciform ligament; 278 has one of its four grooves entirely on the left lobe. The diaphragm in number 71 is still attached to the liver by the coronary ligament and shows alternations of thick and thin bands in the musculature which seem to be mainly due to a readjustment in position of the muscle bundles rather than to hypertrophy. The thicker bands correspond to the grooves and the thinner areas to the eminences. Number 254 had in groove 1 a part of a diaphragmatic fold, the inferior end of which was adherent to the surface of the liver. This suggests a causal relation between a localized peritonitis and the grooves similar to that found in 151.

From a liver much enlarged to one distinctly below the adult average. The right lobe is normal, elongated in a longitudinal or transverse direction, thickened or flattened and is frequently bomb-shaped; the bomb is directed ventrad, cephalad, or laterad or in intermediate directions.

The left lobe is usually normal but in one case nearly equals the right in length and twice reaches to the left lateral abdominal parietes. The Spigelian lobe is pinched and elongated in but one case, the gall bladder in two; in one instance both make an acute angle with the long axis of the body.

Mattei's (1890) record, together with that made here, should alone be used in estimating the frequency of grooved livers, as others fail to give the total number of subjects ex-

TABLE II.

No. of subject.	Sex.	Age.	No. of grooves. Costal.	No. of grooves. Diaph.	Depth. 1. 2. 3. 4. 5. 6. 7. 8. 9.	Length. 1. 2. 3. 4. 5. 6. 7. 8. 9.	Breadth. 1. 2. 3. 4. 5. 6. 7. 8. 9.	Position. 1. 2. 3. 4. 5. 6. 7. 8. 9.	Sides. 1. 2. 3. 4. 5. 6. 7. 8. 9.	Direction of bomb. Superior.	Ventral.	Lateral.	Right lobe elongated.
X	?	?	0	1	.35	3.6	s.	v.	p.				0
A	?	?	2	1	1.	7.5	.35	l.	w. d.	+	+		+
48	♂	43	3	1	1.8	10.	.1	l.	m. d.	+	+		0
89	♂	62	3	1	—	—	—	l.	—		+		+
104	♂	51	2	1	1.	6.8	—	l.	w. d.	+			+
120	♀	*	0	1	—	—	—	v.	—				0
80	♂	78	0	2	1.4 .1	10.7 2.2	.35 —	l. v.	m. d. —		+		0
103	♂	53	2	2	— .3	— 4.	.7	v. l. b. v.	— w. d.		+		0
115	♂	**	0	2	1.5 —	1.9 1.7	.2 —	v. v.	w. d. w. d.				0
76	♂	64	2	3	.1 1.4 1.8	4.3 .8. .8.	— .5 —	l. l. v.	— m. d. p.		+		0
105	♂	68	2	3	.1 .35 .05	2.5 3.3 3.5	— .2 —	d. b. l. v.	— w. d. —				0
112	♂	70	3	3	.2 .9 1.8	8.2 10.9 7.5	— .52 .7	l. l. l.	— m. d. p.	+			+
40	♂	old	2	4	.2 .4 .25 .1	5.5 6.1 6.2 3.1	— — — —	l. v. l. b. v. v.	w. d. w. d. w. d. w. d.		+		0
119	♂	76	1	4	s. .3 .3 .5	1.5 3.7 3.8 4.2	s. .15 — .2	l. v. v. v.	p. m. d. w. d. w. d.				0
85	♂	73	0	5	.4 .4 1.2 1.4 .1	5.1 4.3 7.7 8.1 3.5	.2 .28 .28 .38 —	l. l. l. v. v.	w. d. w. d. m. d. m. d. —		+		0
201	♂	80	0	5	— .7 — .1 .3	2. 5. 2. 1.5 4.5	— .05 — — —	d. l. v. v. v. left lobe.	w. d. m. d. w. d. w. d. w. d.			+	0
151	♀	78	0	9	— — 1.7 .1 .4 1.9 — — .3	3.8 4.6 8.5 4.6 6.1 6.6 4. 3.7 3.9	— — .3 — .25 .5 — — —	v. v. v. v. v. v. v. v. v.	w. d. w. d. p. w. d. m. d. m. d. w. d. w. d. m. d.				0
B	?	?	3	1	.6	3.5	—	v. l.	s.				0
83	♂	51	1	1	1.	8.2	—	v.	w. d.			+	+
C	?	?	2	1	2.	9.5	.2	v. l.	p.				0
279	♂	68	0	1	1.	2.5	s.	l.	s.				0
D	?	?	3	1	.4	5.	s.	v.	w. d.				+
213	♂	80	2	1	1.5	10.1	3.	l.	p.				0
258	♂	68	0	2	— —	6.5 7.	— .2	l. l.	— w. d.		+	+	0
260	♂	40	2	2	1.5 .5	4.7 4.7	— .2	l. l.	w. d. m. d.		+	+	+
254	♂	77	2	2	1.5 1.	9.5 9.7	.5 .2	l. l.	p. m. d.		+		0
283	♂	84	2	2	— .5	4.5 8.	— —	v. l. v.	— m. d.				0
280	♂	85	2	3	.2 .8 .6	2. 7.7 6.1	— .35 .1	l. l. l.	w. d. p. p.				0
305	♂	?	3	3	.4 .6 1.1	7.2 6.8 6.	.2 .35 .25	d. l. l.	w. d. w. d. w. d.			+	0
286	♂	76	3	4	.1 .2 .8 —	5.5 5.7 8.7 5.	.2 .25 .25	d. d. l. d. l. v.	w. d. w. d. m. d. w. d.		+	+	0
278	♂	64	1	4	.1 .2 .1 .3	4.5 3.7 2.5 8.1	— — — .35	d. l. l. l. v.	— w. d. w. d. —		+	+	0
304	♀	71	2	5	— — .6 .2 .8	3. 2. 5.2 3.5 5	— — 2.5 .2 —	l. l. l. l. v.	— — w. d. w. d. w. d.	+	+		0
71	♂	60	0	6	1. .6 .6 .5 .3 —	3.7 4.2 4.6 4.6 4 —	— .2 .2 .2 — —	l. l. v. s. v. s. v. s.	— m. d. w. d. w. d. w. d.			+	0

* fœtus 8 months.
** fœtus at term.
d. = dorsal.
d. b. = dorsal border.
d. l. = dorso-lateral.
l. = lateral.
m. d. = moderately diverging.
p. = parallel.
s. = slit.
v. = ventral.
v. s. = ventro-superior.
v. l. = ventro-lateral.
v. l. b. = ventro-lateral border.
w. d. = widely diverging.
— = too small or too indefinite for exact measurement.
+ = position of bomb or elongation of right lobe.

amined. Adding to his 146 bodies the 68 examined here gives a total of 214, in which 86 grooved livers were found, that is, they occurred in 40 per cent of the bodies. This result will probably be changed when systematic records of thousands instead of hundreds of cases are available. The same limited records give the only adequate data for the determination of sex frequency. The accompanying tabulation shows that grooved livers were found in 53 per cent of the females and 27 per cent of the males. The absolute accuracy of this percentage is further limited by the small number of female subjects autopsied or dissected.

TABLE III.

	Bodies examined.		Grooved livers found.	
	Male.	Female.	Male.	Female.
Mattei	87	59	26	35
Moody	59	9	13	2
	—	—	—	—
	146	68	39	37

Table 2 shows that grooves are found on the ventral surface of the right lobe 30 times, on the lateral 37, dorsal 3, ventro-lateral border 5, dorsal border 1, dorso-lateral border 3, ventro-superior 3. Some of these grooves pass to the superior surface, a few extending upon the dorsal. In two livers, 43 and 151, grooves occurred on the ventral surface of the left lobe and in one, 83, a groove passed from the right to the left lobe. Approximately parallel to each other and to the long axis of the body, the grooves usually have the direction of the overlying muscle fibers and consequently tend to converge at the top and diverge at the bottom. In a single case, 112, one ventral and one lateral groove converged to meet on the dorsal surface. Even in 151 where the two deep grooves converge at both ends the fibers coincide in direction.

The same table also shows that of the 33 grooved livers, 23 were found in adult males, 3 in adult females, 1 in a male, and 1 in a female fœtus, 5 in bodies of which no record was kept. It also shows that most of the subjects are old; 4 between 80 and 90, 5 between 70 and 80, 7 between 60 and 70, 3 between 50 and 60, 2 between 40 and 50. No subjects in youth or infancy are available and only 14 fœtuses. Of the latter there are seven of each sex, their ages ranging from 15 weeks to nine months. Distinctly grooved livers occur in an 8 months' female and in a 9 months' male fœtus and in a 3½ months' female there is a slight bomb and a strong suggestion of furrows. The number of grooves varies from 1 to 9 but, contrary to Buy's observations in which two and three sulci were most common, one occurs most frequently in the adult series. The tabulation shows depth to vary from less than 1 to 19 millimeters but indicates no such relation between depth and position as is suggested by Buy and Jacquemet nor does it show such a constant increase of depth with age as is claimed by Mattei and Buy. The deepest groove occurs in various positions with reference to the others. There is no constant relation between depth, breadth and length, although in general the deepest are longest and narrowest. The length varies from 1.7 to 10.9 centimeters, the bottom breadth from a mere slit to .7 centimeters. In a large proportion of cases the breadth of the grooves increases at the top by the divergence of the walls which sometimes is so great that in shallow grooves no measurements are practicable.

Since the peritoneum is not preserved in embalmed material, its condition cannot be ascertained, but in five cases in which microscopic examination has been made the capsule at the sides and bottom of the groove is thickened, slightly in the shallow and greatly in the deep grooves. Blood-vessels, larger than those usually found, lie in this thickened connective tissue. The parenchyma is degenerated and atrophied at the sides and bottom of the grooves; this process has extended in some cases to include the peripheral layer of liver lobules.

Besides these microscopic changes certain gross pathological conditions are found involving the lungs, pleura, stomach and liver. Owing to the fact that dissection was more or less advanced when the grooves were first noticed, observations on organs other than the liver are not complete. In seven cases the condition of the lungs is recorded, in four of which they were normal, in three tubercular. Eight cases were examined for pleurisy; it was found double in seven, single in one, slight in six, and in three the pleura is adherent to the diaphragm. A bilocular stomach occurred in one case in which there was also a double ureter on the right side. Of the so-called "signs of constriction" the superior bomb is present in 5 cases, the elongated right lobe in 3 of these and 4 others, costal impression in 23, pinched and elongated Spigelian lobe in 1, elongated gall-bladder in 2. Of the 33, 20 have bombs,[4] 7 ventral, 2 superior, 3 lateral, 3 ventro-superior, 5 ventro-lateral; the 12 without bombs include fœtal livers.

Remarks.

The custom of generalizing from a few cases and the desire to establish a certain hypothesis has heretofore often resulted in limiting the horizon of observers and in coloring their interpretations of facts. It is evident that this study can yield no theoretical generalizations, but it suggests some new possible causes in certain cases and presents some interesting evidence which modifies previous interpretations.

In only one case are the grooves so situated that they could possibly be formed by the lower margin of the ribs as demanded by Liebermeister's (1864) theory; moreover in four of the cases there are no lesions of the lungs or pleura that would cause forced respiration. The latter fact has equal weight against Zahn's (1882) view and, as Buy (1904) has pointed out, diaphragmatic folds or digitations are not always present, a condition incompatible with Zahn's (1882) state-

[4] A modification is made of Charpy's term "bombé" which he applies only to livers decreased in transverse and dorso-ventral diameters with a superior protuberance. In these tables and descriptions its use is extended to include livers with lateral and ventral projections.

ment that they must precede the formation of grooves. Further, as Mattei (1890) claimed and Orth (1888) and I have demonstrated, these grooves exist in intra-uterine life.

The occurrence of the sulci on fœtal livers and the presence in adults of thickened muscular bands at the bottom of the grooves and thinned areas over eminences are the only facts found to support Mattei's (1890) theory, but this condition loses its significance when it is remembered that in some of the adult and fœtal subjects the musculature of the diaphragm is of uniform thickness. The existence of grooves without folds is further evidence against this view and moreover if Mattei (1890) is right the eminences are always above and the bottom of the grooves at or slightly below the normal level of the liver surface; whereas in cases 112, 119 and 115 the summits of the mounds are not above this level. Again, in several cases there are in the diaphragm alternate thick and thin bands, which are so far distant from the grooves, that no causal relation can possibly exist. The other theory considering the grooves to be of congenital origin, advanced by Tigri (1873) and based on only three cases, fails to account for those instances in which folds are absent.

A careful consideration of the facts in these cases shows that the constriction theory may account for some but entirely fails when applied to others. Table 2 apparently supports Buy's (1904) claim that grooves occur chiefly in old people but it should be remembered that comparatively few subjects in infancy or youth come to the dissecting or autopsy tables. His statement that grooves are much more frequent in females than in males is also seemingly confirmed but the same fallacy exists in these as in Mattei's (1890) results, that the total number of female bodies examined is comparatively so small that the result does not necessarily indicate the facts. The absence of folds and the evident heaping of the liver tissue in some cases gives a real support to this theory. Opposed to it are the facts that grooves occur upon 4 livers bearing no marks of constriction, and that five livers with acknowledged characters of long continued constriction have no diaphragmatic grooves. Of the constriction signs, designated by Buy (1904) as constantly coexisting, the elongated right lobe is found in only six cases; costal grooves, which may be post-mortem in 23, and a bomb in 19, bilocular stomach once; elongated gall bladder twice and a similar condition of the Spigelian lobe once. But splenic costal grooves, enteroptosis, nephroptosis, transformation of some part of the left lobe into membranous appendices and a partial separation of the caudal extremity of the right lobe are not found. The one insurmountable obstacle to the general application of the constriction theory is the existence of diaphragmatic grooves on fœtal livers. Three such cases are now on record; the youngest fœtus, 7 months, is reported by Orth (1888) and the two others are described in this paper together with the liver of a 3½ months' fœtus with strong suggestions of the beginning of such grooves.

The formation of sulci before birth, at a time when there can be no external pressure by clothing and the organs of respiration are yet inactive, excludes the application of both the constriction and disordered respiration theories to these cases; and the associated uniform thickness of the diaphragmatic musculature renders the hypothesis of Tigri (1873) and Mattei (1890) equally inapplicable. A simple explanation suggests itself as possible. It is well known that the size of the teeth is not always proportionate to that of the jaw so that the former are sometimes very much crowded. Thus it is possible that a similar disproportion between the abdominal capacity and the liver might result in a folding of the liver substance and the formation of grooves.

The associated conditions in 112 and 48 suggest another interpretation applicable to some cases. As already described the diaphragm in both subjects was firmly bound to the right thoracic wall and to the pleura of the right lung by strong adhesions which results in a high insertion and consequent shortening of the diaphragm. Microscopic examination of the folds shows thickened pleura, musculature and peritoneum with adhesion of the infolded layers. These conditions indicate that a severe pleurisy has been followed by the development of scar-tissue which in turn contracts and causes a folding of the diaphragm naturally parallel with the long axis of the muscle fibres and a subsequent grooving of the liver by the folds; that is, the probable cause of these grooves is the pressure of diaphragmatic folds formed mechanically as a result of a severe diaphragmatic pleurisy.

The pathological conditions in subject 151 suggest still another cause for the existence of the grooves. In this case, it will be remembered, a cholecystitis was accompanied by a localized peritonitis and the formation of strong adhesions between the ventral surface of the caudal part of the gall bladder and the diaphragm. One result of this adhesion was the shortening of all the muscle bundles passing through it, another the subsequent contraction of the scar-tissue which caused these and adjacent bundles to converge. The shortening of these fibers would probably result in compensatory hypertrophy, giving rise to thickened bands which by pressure gradually groove the liver.

Conclusions.

Diaphragmatic grooves are found in the fœtus as early as seven months, in infancy, in youth and in old age.

The grooves may or may not contain folds of the diaphragm, the latter are sometimes permanent and sometimes disappear when the liver and diaphragm are removed from the body.

The comparatively small number of cases recorded does not justify definite generalizations concerning the frequency of these grooves and the age and sex of subjects in which they are most often found.

Many factors take part in the production of the grooves, some of which may be congenital conditions of the diaphragm, difficult respiration, constriction of the thorax and abdomen by clothing, severe diaphragmatic pleurisy, localized peritonitis and a disproportionate ratio between the size of the liver and of the abdominal cavity.

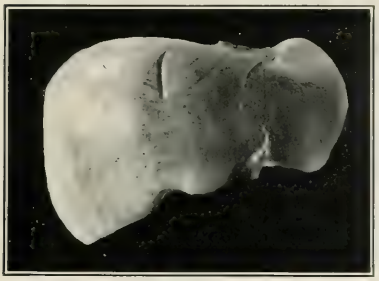


FIG. 1

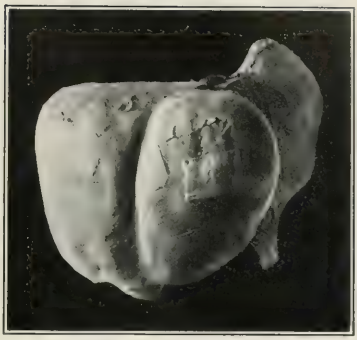


FIG. 2



FIG. 3

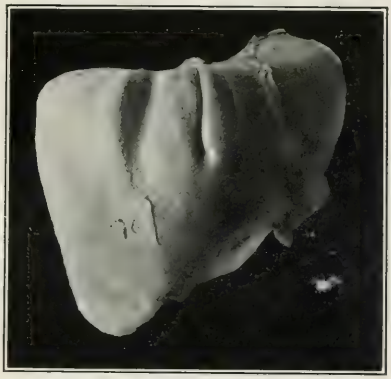


FIG. 4



FIG. 5



FIG. 6.

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THE RISE OF THE PRESENT CONCEPTIONS AS TO THE CAUSE OF THE HEART-BEAT.

II. THE MYOGENIC THEORY, AND MODERN STUDIES OF RHYTHMICITY.[1]

By E. G. Martin.

The myogenic theory of the origin of the heart-beat, as it stands at the present time, is based on four general points. The first of these is the well-established fact that the property of rhythmicity may reside in muscular tissue entirely independently of the presence of nerve-cells. The second point is the demonstration that certain ganglion-free portions of the adult heart may, by proper treatment, be made to beat rhythmically. The third, and according to Engelmann[2] (Pflüger's Archiv, 1897, Vol. 65, p. 535), the most important fact of all, is the conclusive proof that the whole heart of the embryo contracts rhythmically before it contains the smallest trace of nerve tissue. A fourth fact is that the hearts of many invertebrates are without ganglion cells. A fifth fact, which at the time of its discovery was supposed to be absolutely conclusive, but which has been shown in the light of more recent knowledge to be without particular bearing on the problem, was the observation that in animals poisoned with curare, or as it was known at that time, woorara, the heart continued its beat in the normal manner. This poison was supposed by its first user in physiology, Claude Bernard, to sever completely all connection between motor nerves and the muscles supplied by them. Since it does not affect the heart-beat, the conclusion was at once drawn that the heart-beat is not carried on through the action of motor nerves, and hence must be a property of the muscular tissue itself. I find that special stress is laid on this argument as late as 1875. In Flint's text-book of Physiology, published in that year, the author

[1] Read before the Physiological Seminary of the Johns Hopkins University March 2, 1904.

[2] For complete references to the literature of the myogenic theory of the heart-beat see Engelmann, Pflüger's Archiv, 1897, Vol. LXV, p. 535, et seq.

considers the woorara effect as the most convincing of the facts which he presents in support of the myogenic theory. With the discovery that curare affects only one particular sort of nervous end-connection, a form which is not present in the heart, this argument, of course, lost its force.

To return to the four points, which, as I said at the beginning, are at the present time the strong arguments in favor of the myogenic theory, I have found it a matter of considerable difficulty to prepare an account of their historical development, partly because of the great number of names that are associated with each one of them, and partly, also, because they were foreshadowed in the minds of scientists, so that they are suggested in their writings before the actual proof of their truth had been furnished. I shall attempt, however, to give some idea of the way in which each of them reached its present position.

In the year 1850 Schiff, in an article in the Archiv für physiologische Heilkunde, entitled Der Modus der Herzbewegung, makes the following statements: "Many have held the opinion that all forms of rhythmic activity are accomplished only through the medium of nerve-centers. The various ganglia have been looked upon as such centers, but not only plain muscle, but also cross-striated, skeletal muscles, under certain conditions, after destruction of their central organs, or after section of their nerves, or even after removal from the body, have been observed to make repeated contractions, either rhythmic or arhythmic, just as in the case of the heart. Among these are to be included, not only the periodic contractions of small bits of the diaphragm or of the gills of fishes, which can be seen under the microscope as much as thirty-six hours after the death of the animal, and which were discovered by Remak; but also the strong contractions of the diaphragm which occur for a time after section of its nerves, as described by Valentin; and the intermittent movements of the detached legs of insects and spiders, which can be seen with especial ease in Tipula and Phalangium. In ravens, in which I had destroyed the brain and spinal cord, and separated out the great breast muscle, I have seen, sometimes, the pectoralis minor contract strongly and rhythmically, with such great regularity that after I had determined the interval between the contractions, I could foretell the onset of every one by counting with a watch. These contractions continued after I had separated the muscle, with its adherent portion of the skeleton, from the rest of the body. I cut the ribs, with the intercostal muscles attached, from the body of a young cat, and hung them on a frame. I observed that the ribs, through the rhythmic contractions of the muscles, came together and separated like the slats of a venetian blind. And all these parts, whose rhythmic action was not disturbed by the destruction of their nerves, nor by separation from the body, contained only red, cross-striated muscles, only animal nerve-fibers, with not a ganglion in their substance. Indeed the leg of Phalangium opilio begins its regular movements, and the tail of Lacerta its irregular ones, only at the moment of separation from nerve centers. The heart may well be continuously under just those conditions into which the muscles we have been considering are brought through the experiment, and it can by no means be asserted that the regular rhythm of this organ is necessarily dependent on the existence of nerve centers."

Shortly after the appearance of this paper of Schiff, with its description of the experimental production of muscular rhythmicity, if so his phenomena may be called, statements of the normal occurrence in the animal body of similar muscular rhythmicity began to appear in scientific journals. In 1852 Wharton Jones showed that the veins of the bat's wing contract rhythmically. Schiff, himself, in 1854, described the rhythmic pulsations of the vessels of the rabbit's ear. Several years later, in 1869, Engelmann discovered the fact that the ureters are rhythmically contractile. In each of these cases it was shown, either by the first one to observe it, or by subsequent investigators, that ganglion cells are not present in these tissues. These observations demonstrated beyond question that the power of executing rhythmic contractions may reside in muscular tissue entirely apart from the influence of nerve-cells. While these observations had no direct bearing on the question of the origin of the heart-beat, they were of the very greatest value as indirect evidence, because they made the probability of the muscular origin equal to that of the nervous origin, thus robbing the latter of the greatest advantage it had held up to this time, the proven possibility of nervous rhythmicity, against undemonstrated muscular rhythmicity.

As early as 1858 the observation was made by Eckhard that if a constant current were sent through the apex of the frog's heart, a portion which had been shown to be free from ganglion cells, it would be thrown into rhythmic contractions. Foster and Dew Smith, in 1876, made the same observation. Bowditch, in 1871, and Merunowicz, in 1875, both working in Ludwig's laboratory, showed that the apex of the frog's heart would beat when supplied with a nutrient fluid under pressure. Gaskell, in 1880, proved that a ventricle which had been brought to rest by Bernstein's crushing, could be aroused to activity again by the simple process of clamping the aorta, thus raising the pressure within the chamber. Three years later, in 1883, Gaskell reported that if a strip were cut from the ganglion-free apex of the heart of a tortoise, and suspended under slight tension in moist air, it would begin, after a while, to contract rhythmically, and might remain active for as much as thirty hours. He stated also that the onset of rhythmic activity in an isolated strip could be hastened by the application of stimuli to it at regular intervals. It should be stated that more recent work has not corroborated the statement of Gaskell that strips of heart tissue will develop a spontaneous rhythm when suspended in air without previous treatment, but this modification does not affect his point, which was that the muscular tissue of the heart could be made to beat without the influence of nerves. In 1882 Engelmann showed that the bulbus arteriosus of the frog can be made to beat with great readiness, all that is required being a slight and continuous tension of its walls. He claimed that this part of the heart is without nerve-cells, and

his view seems to find general acceptance, in spite of the fact that one or two observers, Munk (1878), Löwit (1881), and others, have reported their presence. Engelmann also, in 1896, showed that parts of the venous sinus of the frog which are free from ganglion cells could be isolated, and that they would continue to beat for a long time after isolation. As is well known, the normal beat of the heart originates in the region of the great veins, hence, as Engelmann points out, the fact that those parts of them that are not furnished with nerve-cells beat as well as those that contain such cells, is the strongest kind of indication of the correctness of the myogenic theory.

In 1865, A. Brandt, working in St. Petersburg, reported that the hearts of certain crabs, of some species of insects examined by him, and of some molluscs also, are without ganglion cells. The same thing was afterward shown to hold for other invertebrates by Eckhard (1866), Foster (1872), and Foster and Dew Smith (1875).

There remain to be considered in this connection, the facts with regard to the beat of the embryonic heart. It has been a matter of common observation for a very long time that the hearts of embryos, such as the simple heart tube of the unhatched chick, begin to pulsate rhythmically early in the life history of the developing animal. The Weber brothers performed some experiments, such as the effect of variations of temperature and the like, upon the heart tubes of embryo chicks. About their time, the middle of the nineteenth century, the idea began to be entertained that these heart tubes contain no nerves. Such was the indication furnished by the microscope, although with the technique at their command the investigators of that day were unable to prove it. The first positive statement on the subject, which I have encountered, was made by Pflüger in 1877. He found that the heart of the human embryo begins to beat after the third week, whereas no nerve-cells are to be found in it until the fifth week. With the development of modern methods of studying tissues, by means of which every infinitesimal particle of an organ can be scanned with unerring accuracy, the question as to whether or not pulsating embryonic hearts contained nerve-cells, was finally settled. The most complete study of this point was made by W. His, Jr., in 1891. This observer showed that the heart of Scyllium began to beat when the embryo had attained a length of five millimeters, although nerve-cells did not appear until a length of thirteen millimeters had been reached. In the chick the heart-beat after thirty-six hours, while the first indications of ganglion cells appeared only on the sixth day. The upholders of the neurogenic theory explained the beat of the embryonic heart by supposing that embryonic heart tissue was in an undifferentiated form, combining in itself the properties of both muscle and nerve, which properties became gradually separated from each other with the development of the two different adult forms out of the same sort of embryonic substance. His, however, was able to follow the process of development of the embryonic heart, and to demonstrate beyond doubt that all the tissue there present grew into the characteristic, cross-striated muscle substance of the adult heart. He showed, moreover, that the nerve-cells which appear in the heart wander there from the cerebrospinal nervous system. The neurogenists, overthrown in this idea, advanced another argument. They suggested that while it must be admitted that the beat of the embryonic heart is myogenic, there was still good reason to suppose that a transition of control occurs at some point during development, so that the beat of the adult heart becomes nervous. Engelmann points out the difficulty of accepting this proposition, both in view of the fact that the heart, from the very commencement of its activity, beats regularly, without any disturbance such as would inevitably accompany a change in its manner of control, and also in the light of his own observations on the rhythmicity of ganglion-free portions of the great heart-veins.

Gaskell[3] has recently proposed a very satisfactory explanation of the normal sequence of the heart-beat, basing his explanation upon the idea that a distinctive property of embryonic heart tissue is a very high degree of irritability. Let me here quote his own statement of his view. Having called attention to the fact that certain parts of the heart, i. e., the venous sinus, the auriculo-ventricular ring, etc., are more rhythmical than the rest of it, and that this superior rhythmicity has been supposed to be due to the presence in those parts of nerve-cells, he proceeds as follows: "But is there really nothing else peculiar to those parts where rhythm is easiest? If we consider its mode of development, we find that in all vertebrates the heart arises from two longitudinal veins, or venous sinuses, which coalesce to form the sub-intestinal vein and heart; the simple tube so formed, with its circular muscular coat, becomes twisted on itself, and parts of it develop bulgings, the commencement of the auricles and ventricles, in consequence of which the simple circular arrangement of muscle fibers becomes the complex arrangement which is ultimately found. With this special growth of the parts of the tube by which the heart cavities are formed, is correlated a more rapid contraction of the specialized parts of the muscular walls, so as to ensure a more rapid emptying of the separate cavities, and thereby make the heart more efficient as a force pump. The development of this nearer approach to striated muscle is made at the expense of the original rhythmical power, so that finally the muscular tissue of the heart becomes differentiated into muscle of varying rhythmical power, according to the amount of deviation from the original embryonic rhythmical muscle. Those parts which remain least altered, both in the circular arrangement of their fibers and in their physiological status, are naturally the large veins, sinus, and junction of sinus and auricles; then the circularly arranged fibers of the auriculo-ventricular groove; and lastly the conus arteriosus, which represents the final part of the tube beyond the ventricular bulging. In fact, as can be readily understood, if the auricular and ventricular bulgings are special modifications of the muscular tissue, for the purpose of forming rapidly-contracting roomy chambers—in other words, for

[3] Gaskell, Schaefer's Physiol., 1900, Vol. II, p. 177.

the purpose of forming a heart rather than a rhythmically contractile tube—then the very parts which were left unmodified would naturally continue to carry the main intracardiac nerves with their accompanying ganglion cells; so that in the sinus, in the auricles, and in the auriculo-ventricular ring, the ganglionic structures and the less modified muscular tissue would be coterminous." It should be stated that although this idea was developed to its fullest extent by Gaskell, others before him had held the same view. Michael Foster, as early as 1876, made a similar suggestion to explain the greater rhythmic power of the venous portion of the heart.

Only one more point remains to be considered in this immediate connection. It will be recalled that as late as 1894 Kaiser put forth a very strong argument in favor of the neurogenic theory. His argument, to recapitulate briefly, was this. It is well known that if a frog's heart be brought to rest by tying off the sinus, single stimuli applied generally to the surface of either auricle or ventricle are followed by only a single response for each stimulation; whereas, if the stimulus be applied in the region of Bidder's ganglion in the auriculo-ventricular ring, each single stimulation is followed by a series of rhythmic contractions. Moreover, he showed that if Bidder's ganglion were removed, stimulation in the region which before had aroused a series of responses, now, like the structure generally, gives only one response for each stimulus. He drew the conclusion from these results that in nerve centers, such as Bidder's ganglia, and in them alone, resides the power to arouse rhythmic contractions in the heart. The error in Kaiser's argument was brought out by Gaskell,[4] who showed that Kaiser's experiment had not been performed with sufficient care. Gaskell showed that if the ventricle and one auricle in the heart of a tortoise be slit and pinned back in such a manner as to expose fully the inner surface of the septum and auriculo-ventricular ring, together with Bidder's ganglia and the terminations of the vagi in them, the whole of the region about those parts could be explored with a fine-pointed needle. Under these conditions Bidder's ganglia may be pierced with the needle, or pulled upon, or stimulated otherwise as violently as one wishes without arousing a single contraction; but if the muscular tissue of the surrounding auriculo-ventricular ring be touched, never so lightly, a series of rhythmic beats immediately ensues. According to Gaskell's view of the embryonic nature of the auriculo-ventricular ring, which should, as the result of its embryonic nature, retain its property of rhythmicity to a high degree, the result he obtained was the only one to be anticipated. The apparently contradictory result obtained by Kaiser, he explained as due to insufficient care on the part of that observer in limiting his stimuli to the ganglia, in the one case, and in removing the ganglia without at the same time destroying the muscular portion of the auriculo-ventricular ring, in the other.

This work of Gaskell practically completed the chain of evidence in favor of the view that the rhythmic action of the heart does not originate in the ganglion cells. His results, however, apply only to the cold-blooded heart. The proof was extended so as to include the mammalian heart by Porter in 1897. He perfused the ganglion-free apex of a dog's heart, according to a modification of the method devised in this laboratory by H. Newell Martin, and obtained an excellent series of well-sustained, long-continued, contractions; proving, thus, that in the mammalian, as well as in the cold-blooded heart nerve-cells are not essential to rhythmic activity. A number of observers have argued that the nerve-fibers, which penetrate the heart tissue everywhere, may be the source of its rhythmicity. The most prominent upholder of this view was Schiff (1850). He seems to have adopted it, after becoming convinced that nerve-cells could not be the efficient source, as the next best hypothesis. Although there is some evidence that under certain circumstances peripheral nerve-fibers may convert a constant stimulus into a rhythmic one, the belief that the rhythmicity of the heart is brought about in this way, has nothing with which to commend itself to us, as compared with the great mass of evidence favoring the myogenic theory.

Having now, I hope, succeeded in giving some idea of the rise of the theory of the heart-beat which prevails at the present time, I wish to pass to a brief discussion of the studies that have been made with regard to the influence which nerves do have upon the heart's activity; following that, and closing my paper, with some account of the work that has been done on the question of the conditions under which the heart's rhythmicity is maintained.

Mention was made in my last paper of the discovery of cardiac inhibition by the Weber brothers in 1845. Their idea of the mechanism by which it is effected, was based, it will be remembered, upon their belief in the ganglionic origin of the heart-beat. They explained cardiac inhibition simply as a special instance of the inhibitory action of a nerve upon a motor ganglion. The rise of the myogenic theory compelled the abandonment of this simple idea, and various hypotheses were proposed to account for the effects of vagus stimulation. Not the least curious of these was the one advanced by Schiff[5] (1849). This author rejected the idea of inhibition altogether. He looked upon the vagus as the true motor nerve of the heart, but believed that its ordinary function was exercised through the medium of excessively feeble stimuli. As was suggested in another connection, he thought that the constant stimulus which was carried by this nerve was transformed into a rhythmical one through some intrinsic property of the terminal nerve-fibers themselves. Since, according to his view, the usual impulse carried by the vagus is a very feeble one, it ought to be possible for strong stimulation to produce a condition of exhaustion much more promptly than in a nerve which is adapted to the transmission of strong impulses. He looked upon vagus inhibition as such a case of exhaustion from overstimulation. In support of his contention he cited the fact that weak stimulation of the trunk

[4] Gaskell, loc. cit., p. 179.

[5] Schiff, Arch. für physiol. Heilkunde, 1849, Vol. VIII.

of the vagus in the frog, frequently resulted in acceleration rather than inhibition. He likewise quoted this experiment of his own in favor of his view. He stimulated a small area of the surface of the ventricle electrically, and observed that the stimulated area remained in a relaxed condition throughout the contraction of the heart as a whole. This "local diastole" he attributed to exhaustion of the stimulated area, equivalent to that which resulted on a large scale from overstimulation of the motor nerve of the whole heart, the vagus.

We owe our most satisfactory hypothesis of the action of the vagus in terms of the myogenic theory of the heart-beat, to Gaskell.[6] This author calls attention to the fact that vagus stimulation not only slows the rate of the heart's beat, with a tendency to bring it to rest, but also diminishes the force of the individual contractions, and depresses both the excitability and the conductivity of the tissue. These facts, he says, show clearly enough that the vagus effect must be some sort of direct peripheral inhibition of the muscular tissue itself. If the action were through inhibition of some source of stimulation, the force of the beat would not be affected when the inhibitory nerve was stimulated, because, as is well known, the heart responds to stimulation according to the "all or none" law; hence weakening the stimulus could not have any effect on the force of the beat unless it became pronounced enough to stop the heart altogether. Moreover, the fact that vagus inhibition depresses both the excitability and conductivity of the tissue, is another strong indication that the action of this nerve is directly upon the muscle substance itself. The way in which the inhibition acts upon the tissue, he does not undertake to say; nor has any one offered more than the most tentative suggestions as to the mechanism of this most interesting nervous action. Gaskell has advanced other ingenious views as to the function of the vagus nerve, which the time at my disposal will not permit me to consider.

The Webers had some vague notion of what we know as cardio-acceleration. They looked upon the sympathetic nerves to the heart as possessing a function just the opposite of that exercised by the vagus, but their idea was not made the subject of rigid experimental study, so the true discovery of cardio-acceleration did not come for some years after their time. The fact that weak stimulation of the vagus often produces acceleration had been noted repeatedly, but only to create confusion in the minds of those who were trying to find a satisfactory explanation for the phenomena of inhibition. However, in 1867, v. Bezold,[7] working upon mammals, showed that stimulation of the cervical end of the cord, sectioned in the upper thoracic region, always produced pronounced acceleration under favorable circumstances, without necessarily increased blood-pressure. He had observed the increased pulse rate on stimulation of the cervical cord, some four years before, but Ludwig and Thiry pointed out that his effect might be due entirely to vasomotor changes. His last experiment excluded these by section of the cord, just below the point of stimulation; thus he was able to establish his discovery beyond question. In 1867 the brothers Cyon[8] showed that the course of the accelerator fibers must be by way of the stellate ganglion, and finally Schmiedeberg and Ludwig,[9] in 1871, traced the full course of the accelerator fibers in the dog. No more is known of the mode of action of these nerves than of the inhibitors. Gaskell points out that they exert, in general, precisely the opposite effect from that exerted by the inhibitory nerves.

The study of the conditions upon which the rhythmicity of the heart depends, began in Ludwig's laboratory, with the invention of the "frog-heart manometer" and of the means of perfusing the heart at pleasure with any desired solution. So intimately was the work of Ludwig himself associated with that of his pupils, that it is impossible to assign to each his exact part in the development of the method. Although the various publications in which the early researches along this line appear, bear as a rule the name of the pupil only, it is certainly safe to assume that the inspiration of the master's genius had much to do with the results recorded in them. As the story goes, the first perfusion apparatus was devised by E. Cyon, in the middle sixties, and consisted merely of a bowed tube, tied at one end into one of the great veins of a frog's heart, and at the other into the bulbus, and connecting by a short side branch with a small manometer. This system was filled at first with pure serum, which was pumped around and around through the heart, and the action of the organ observed by means of the manometer. This simple apparatus was quickly modified and improved, an inflow and an outflow reservoir took the place of the bowed tube, thus making the handling of the perfusing solution easier, and making it possible to control the flow of the liquid through the heart. Kronecker devised the well-known perfusion cannula, having two tubes in one in such a way that only the one tube had to be tied into the heart, and yet perfect circulation could be maintained through it. Further detailed reference to the various modifications and improvements that were made in the apparatus for studying the heart, need not be made here, because the most important of them are still in constant use in all laboratories of physiology. In spite of the argument of Kürschner against the possibility of the chemical nature of the blood having anything to do with its action upon the heart, to which I referred in my former paper, the studies of this time were wholly concerned with the chemical influence of the blood, the question as to the relative influence of its different constituents being the one which pressed for an answer. The value of certain mechanical factors, such as pressure, received due regard, but there was no doubt that the chemical structure of the blood was of paramount importance.

The problem as to the exact nature of the chemical influence of the blood upon the heart was taken up in Ludwig's labora-

[6] Gaskell, loc. cit., p. 213, et seq.

[7] v. Bezold, Untersuch. a. d. physiol. Lab. in Würzburg, 1867, Bd. II.

[8] Cyon, Arch. f. Anat., Physiol., u. wissen. Med., 1867.

[9] Schmiedeberg and Ludwig, Ber. d. k. Sächs. Gesell. d. Wissensch., Leipzig, 1870.

tory, about the year 1874, by Kronecker and Stirling,[10] and independently, in the same laboratory, by Merunowicz.[11] Curiously enough, these investigators, working side by side, came to very opposite conclusions, and, in fact, founded two opposing schools. Kronecker and Stirling observed that a frog's heart perfused with sodium chloride solution, beat with gradually diminishing force and finally came to rest; but that if it were perfused with serum, when in this exhausted condition, a prompt and long continued recovery ensued. The natural conclusion to which they came was that the washing with the saline had removed the nutrient materials of the serum, hence the heart was unable to beat until they were restored to it by fresh perfusion with serum. This experiment convinced these observers that the heart's activity depends on the presence in it of a continuous supply of nutritive proteid material. Merunowicz studied the effect of perfusing the heart with a solution of the ash of serum in place of the simple saline solution of Kronecker and Stirling. He found that the heart, perfused with this solution, did not exhibit the decline of vigor noted by those observers who worked with media containing only sodium chloride, but continued active for a long time. He noted that the ash of serum was quite alkaline, and to this feature he attributed the long continuance of the beat of the heart studied by him, and to its absence the quick decline of the heart in sodium chloride. The recovery seen by Kronecker and Stirling upon perfusion with serum was due, according to this view, merely to a renewal of the supply of alkali. It will be convenient to consider separately the development of these two schools, the one looking upon a continuous supply of proteid material as the immediate condition of rhythmic action, and the other, although not denying the ultimate dependence of the heart upon organic food stuffs, laying the greatest stress upon certain of the inorganic constituents of the blood as the intimate necessity for the beat of the heart.

In 1878 McGuire,[12] working under Kronecker's direction, added a few facts to the discussion, although they were not of overwhelming importance. He showed that serum diluted with salt solution is an excellent medium for sustaining the beat of the frog's heart, also that serum is to be preferred to either whole or laked blood. Martius,[13] in 1882, offered a really strong argument in favor of Kronecker's view. He supposed the condition of things to be as follows: the heart is to be looked upon as depending upon the presence of proteids (serum albumin) for its power to beat. The proper assimilation of the proteid by the tissue goes on, however, only in the presence of an alkali; the decline in saline solution, then, does not mean exhaustion of the supply of serum albumin, but merely the undue accumulation of acid CO_2, which interferes with the nourishment of the tissue. The revival which follows the use of the ash of serum or any other alkali, means only the restoration of the power of the tissue to assimilate. According to this idea, the tissue is not exhausted of its supply of blood proteid until it comes to rest in an alkaline salt solution. According to Kronecker's theory, the only thing which could revive the heart after this would be to supply it with serum albumin, and this Martius proved, or thought he did. He showed at any rate, that a heart after coming to rest in an alkaline medium was revived by being perfused with serum. Von Ott,[14] writing in 1883 in support of Kronecker's theory, reached some curious conclusions. It should be stated in order to make his work clear, that Gaule,[15] several years earlier, had reached the conclusion that peptones are very favorable to the heart's activity. Von Ott showed that this idea was entirely erroneous. He found, however, that after a dog was fed on this perfectly indifferent peptone, the stomach contents, even after dialysis, exerted a highly favorable influence on the heart-beat. Believing with Kronecker, that this favorable action was a sign of the presence of serum albumin, he thought that he had not only proven that serum albumin is synthesized from peptone in the alimentary tract, but that he had also obtained a most delicate method of detecting the presence of small quantities of serum albumin. He applied his test to milk and came to the conclusion that it contains this proteid, since its action on the heart is favorable. Dialysis did not diminish the action of milk any more than it had in the case of the stomach contents, so he concluded that the influence of the salts is nil in this instance also. The work of v. Ott was repeated and confirmed four years later by Frl. Popoff,[16] and a little later still by Frl. Brinck.[17] This latter investigator observed that although the ordinary forms of serum albumin have the favorable action on the heart, that prepared pure by the method of Hammarsten is without action on the organ. About this time, the Kronecker hypothesis began to be subjected to such severe criticism, and so many convincing experiments in opposition to it were being reported, that its supporters rather subsided into the background, and since 1895 only two papers of importance in support of it have appeared. The first of these was by White, in the Journal of Physiology, in 1896. This observer stated that the nutritive influence of serum albumin could be demonstrated readily enough. All that was necessary was to treat the heart with the most favorable inorganic solutions until it no longer beat in them, and then transfer it to a solution containing albumin, when, according to White, a good revival would result. As will be shown later, this result was shown by other workers not to be so conclusive as White thought it was. Göthlin,[18] quite recently (1901), has advanced some evidence in favor of the idea that a compound of paraglobulin with lecethin, such as is obtained when serum is diluted, may have some direct

[10] Kronecker and Stirling, Ludwig's Festschr., 1874, p. 173.

[11] Merunowicz, Arbeiten a. d. physiol. Anstalt zu Leipzig, 1875, p. 132.

[12] McGuire, Archiv f. Anat. u. Physiol., 1878, p. 231.

[13] Martius, ibid., 1882, p. 543.

[14] v. Ott, Archiv f. Anat. u. Physiol., 1883, p. 1.

[15] Gaule, ibid., 1878, p. 291.

[16] Popoff, ibid., 1887, p. 345.

[17] Brinck, ibid., 1887, p. 347.

[18] Göthlin, Skand. Arch. f. Physiol., 1901, p. 1.

nutritive value to the heart. His results, however, are not very positive.

We have left to consider the work of those who, with Merunowicz, looked upon the inorganic constituents of the serum as the true source of the heart's normal stimulus. The first to follow in the footsteps of this observer were Gaule[19] and Stienon,[20] both working in the same year, 1878. Both these workers emphasized the beneficial effects of alkalinity, and both believed that the heart could work at the expense of its own substance. These studies of the effect of alkalinity were soon to give place to others in which the different metallic bases of the serum were to become the subjects of investigation. The impulse to this work was given by the English physician, Sidney Ringer,[21] and to him, also, belongs a considerable portion of the credit for developing the subject to its present standpoint. In Ringer's first experiments on this point he made up a solution of sodium chloride in ordinary hydrant water, and observed that it had a tendency to throw the heart into a condition of tonic contraction. He found that this contraction could be overcome by the addition of a small proportion of potassium chloride to the solution. He found that this mixture of sodium and potassium chlorides in solution was very favorable to the heart's activity. His account of this set of experiments appeared in the Journal of Physiology in 1880. His attention was soon, however, directed to the fact that he had not used sufficient care in making up his solutions. He then examined the water with which his solutions had been made up, and found that it contained a considerable proportion of calcium salts in solution. This discovery obliged him to repeat his former work, which he did with the well-known result that he demonstrated the action of calcium to produce tonic shortening in the tissue, and also proposed as a good solution for use in irrigating hearts, the one containing calcium, sodium, and potassium salts, which has since been known by his name. It was quickly shown by Ringer and others that hearts perfused with his solution continued active fully as long as in the best experiments with serum perfusion. This result made it clear that if the heart has any immediate dependence upon the serum content of the blood, that dependence is by no means so apparent as its salt requirement is. The problem, at this point, assumed a two-fold nature. The mode of interaction of the salts of the serum was to be studied, and it was to be definitely determined whether or not any organic substances are immediately essential to the heart's activity in the sense in which the salts are. These studies were prosecuted with vigor both in England and in this country.

A number of papers have appeared from time to time in which the attempt has been made to prove that one or the other organic substance added to a Ringer's solution, improved it as a sustaining medium for the cold-blooded heart. Ringer himself thought that small additions of blood, serum, milk, or whey kept his hearts in activity longer than his inorganic solution alone. He was careful to point out, however, that the presence of the salts was the prime requisite for maintaining rhythmicity. He pointed out incidentally in this connection, that dialysis of blood or milk does not rid them of their calcium content, hence the favorable result of v. Ott with these substances was to be explained as due to the calcium which remained in them after dialysis. Heffter,[22] in 1892, and a year later Albanese,[23] concluded that viscosity was an essential feature of a satisfactory nutritive solution. They therefore recommended gum-arabic as a good substance to be included in the solution. As a matter of fact, the addition of this gum to saline solution improved it as a nutritive medium, but as Howell pointed out, this is due to the fact that gum-arabic is a calcium compound, rather than to any physical property it possesses. Locke,[24] in 1895, although denying the usefulness of gum-arabic, thought that some organic substance would be beneficial, and came to the conclusion that dextrose is such a substance.

Howell's first paper upon this subject, in 1893, took the opposite ground. In collaboration with Miss Cooke,[25] he undertook to make a comparative study of the nutritive value of the different blood-proteids, by determining their relative influence in prolonging the beat of the heart when perfused with nutritive solutions. These authors found, however, that addition of either of the blood-proteids had no measurable effect in prolonging the activity of the heart. They tried to get at the question in another way, by determining quantitively how much proteid was used up by the heart in the course of a long perfusion, but were unable to demonstrate any disappearance of proteid under these conditions. This paper also disposed effectually of v. Ott's idea that serum albumin is synthesized from peptone in the digestive tract, by showing that the beneficial effect of stomach contents is due to the salts, especially of calcium, contained in them. Eaton,[26] at this same time, showed the importance of calcium in another way. He found that if the calcium were precipitated out of the solution by the addition of a little sodium oxalate, its great value as a nutritive medium was lost, but that it returned again with the addition of an excess of a calcium salt. As furnishing practically final proof of the predominant importance of the salts in sustaining the rhythmic action of the heart, the papers of Howell[27] and Greene[28] in 1898 should be quoted. The observations recorded in these papers were made upon the terrapin. It had been supposed by those who favored the view of Kronecker, that enough serum remained in the spongy cavities of the heart to account for the long-continued

[19] Gaule, loc. cit.

[20] Stienon, Archiv f. Anat. u. Physiol., 1878, p. 263.

[21] For the papers of Ringer see the Jour. of Physiol. from Vol. III to Vol XIV.

[22] Heffter, Arch. f. exp. Path. u. Pharm., 1892, p. 41.

[23] Albanese, ibid., 1893, p. 297.

[24] Locke, Jour. of Physiol., 1895, p. 332.

[25] Howell and Cooke, ibid., 1893, p. 198.

[26] Eaton, foot-note to Howell and Cooke, loc. cit.

[27] Howell, Amer. Jour. of Physiol., 1898, Vol. II, p. 47.

[28] Greene, ibid., 1898, p. 82.

activity so frequently observed in inorganic solutions. The work of Howell and Greene was to test this point. Howell showed that the venous portion of the heart, although entirely without any thickness of tissue or spongy structure, conducted itself in inorganic solutions very much as does the heavier ventricle. Long and well-sustained series were obtained from venous strips without the employment of any organic substance whatever, save that contained within the tissue. Greene demonstrated that the ventricle could not require a constant supply of serum albumin by calculating the amount of it which would be used up in doing the amount of work performed by a heart on an inorganic diet, and showing that more would be required than could be supposed, on the most liberal estimate, to lurk in the cavities of the heart, after the thorough washing out to which it was subjected. Finally Walden[29] showed that the experiment of White, in which he revived a heart by serum after it ceased to beat in Ringer's fluid, could be reversed. A heart that would no longer beat in serum could be revived by perfusion with inorganic Ringer's solution.

At the present time the ability of the heart to continue active for a very long time on a purely inorganic diet is generally conceded. The question as to the relative importance of the different constituents of Ringer's solution, in maintaining the beat of the heart, is now the subject of much discussion and a great deal of experimental study. Any consideration of this question would be out of place in a purely historical presentation such as this aims to be.

[29] Walden, Amer. Jour. of Physiol., Vol. III, p. 123.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

October 9, 1905.

Dr. W. G. MacCallum was elected president for the coming year and Dr. C. H. Bunting was elected secretary.

Bilateral Exostoses on the Inferior Surface of the Calcaneus, Gonorrhœal in Origin (Pododynia Gonorrhoica). DR. BARKER.

This man, twenty-nine years old, a weaver by trade, entered the hospital complaining of inability to work, owing to soreness in the lower extremities. Up to two years ago he enjoyed fairly good health, with the exception of the ordinary diseases of childhood, and of a malarial attack at the age of fifteen. About two years ago, while at work, he was suddenly seized with a sharp pain in the lower part of the abdomen; it radiated to the end of the penis, but as far as the patient can remember, did not run down the thighs or into the back. At about this time he passed bloody urine occasionally and was so ill that he was prevented from working. He denies venereal infection, but the attack just mentioned may have been due to gonorrhœa. Shortly after this attack the patient began to have soreness in the bottom of his feet. This soreness extended, he says, into the legs and thighs, and finally affected the back. Two months after the onset of the soreness he gave up his work for eight weeks, but returned to it again and worked until nine months ago, when the trouble became so serious that he was compelled to desist. Some eighteen months ago he had a very severe attack of "sore eyes," and three months ago one of his eyes was again much inflamed. Ophthalmoscopic examination by Dr. Randolph since entrance to the hospital reveals a previous iritis of severe grade in both eyes.

On examination the patient is seen to be rather a spare man, under-nourished. He stands and walks with great difficulty, owing to pain, especially in the back part of each foot. The peculiarity of his gait is due to his effort to keep the pressure off the painful part of the feet. The lower extremities are somewhat atrophied, but probably not more than the disuse accounts for. The examination of sensation reveals no abnormalities. The motor power is nowhere involved. The deep reflexes are, however, markedly increased, especially in the lower extremities; the knee-kicks are very active, and a slight patellar clonus can sometimes be obtained on the left side. The Babinski phenomenon cannot be elicited, nor is Oppenheim's sign present. The mechanical excitability of the muscles is increased, and there is marked dermatographia.

No sufficient evidence of organic disease of the nervous system has as yet been found in the case. There is marked tenderness on pressure on the plantar surface of the foot near the heel on each side. Dr. Cole suggested the possibility of gonorrhœal exostoses, such as have been found in the cases which Dr. Baer has been studying of late. Dr. Thomas, who saw the case also with especial reference to the nervous symptoms, favored this diagnosis. The patient was accordingly sent to the X-ray room, and the negatives which I now pass around were made by Dr. Baetjer. They leave no doubt as to the condition. An exostosis is easily visible on the calcaneus of each foot. It has the typical "worm-eaten" appearance, so often found in these cases; the appearance, Dr. Baetjer informs me, is that of gonorrhœal rather than of syphilitic bony growth.

I should like to draw the attention of the society to the exact position of the exostoses in this patient. It will be noted that the new growth is situated, not on the tuber calcanei, but in front of it, and the exostosis is not connected with either the medial or lateral process of the tuber. On the contrary it projects from the prismatic body (corpus calcanei) of the heel bone. In this position it can scarcely have anything to do with the attachment of the aponeurosis plantaris, which is situated more posteriorly. The exostosis lies more

nearly in the position of the attachment of the posterior extremity of the ligamentum plantare longum, or possibly in the region of origin of the M. abductor digiti quinti on the inferior surface of the calcaneus. Nor can the exostosis, in this case at any rate, be connected with a bursa, inasmuch as the only bursa occurring in this part of the foot is the bursa subcutanea calcanea, which lies just beneath the skin on the inferior surface of the tuber calcanei. I mention this point inasmuch as I understand that in some of Dr. Baer's cases and in other cases which have been reported, the exostoses correspond more nearly to the attachment of the aponeurosis plantaris; a relation to the bursa has also been postulated in certain instances.

We shall refer this patient to Dr. Baer for removal of the exostoses, after which we shall expect him to regain his health.

The increased reflexes and increased mechanical excitability of the muscles are in all probability neurasthenic symptoms which will disappear under suitable treatment.

Dr. Baer, in discussion, told of six cases from his clinic in the last three years, from two of which he got gonococcus in pure culture and from two the stained organism in section. One case was not operated on, and one showed no organisms. These cases were all bilateral, in males, and within one year after urethritis.

Perichondritis, Probably of Gonorrhœal Origin. Dr. Barker.

The patient, a Polish cigarmaker, twenty-seven years old, was admitted to Ward F on September 29, 1905, complaining of rheumatism, and of swelling in the neck. He had applied on August 31 to the genito-urinary dispensary for treatment of an acute urethritis contracted a few days earlier. Gonococci were at that time present in the urethral discharge. On September 18 he began to have pain in the right shoulder and in the right hip. The shoulder became hot, tender, and swollen, and for four days he was unable to put on his coat. Pain then appeared in the right knee, and since that time the metacarpophalangeal joints of the left hand, the metatarsophalangeal joints of the right foot, the left knee and the right ankle have all been painful.

Four days before the present admission the patient noted swelling of his Adam's apple and felt pain, which radiated down the wind-pipe. He had some difficulty in swallowing, but no difficulty in respiration, nor was there any change in his voice. He has complained also of slight stiffness in his right jaw-bone. There has been but little effusion in the joints, with the exception, possibly, of the right shoulder joint at the onset of the attack. The blood presents a moderate grade of secondary anæmia. There are still a few pus-cells in the urine, but otherwise the urine is negative. Dr. Warfield has made a laryngoscopic examination, and finds nothing abnormal inside the larynx. There is no enlargement of the tonsils.

Palpation of the larynx reveals tenderness and slight swelling on the upper margin of the right lamina of the thyreoid cartilage, a little in front of the superior thyreoid tubercle. There has also been tenderness over the right side of the cricoid cartilage, and at present the patient complains when the cartilages of the trachea are pressed upon. There is no superficial redness. The hyoid bone is not tender. No changes can be made out in the thyreoid gland. Otherwise the examination is negative.

The occurrence of perichondritis following gonorrhœa is of interest. Coming on in close association with gonorrhœal arthritis it seems very probable that this perichondritis is gonorrhœal in origin, though the absolute proof (demonstration of gonococci in the lesion) is wanting. Dr. Cole, who has recently been reviewing the literature of the complications and sequelæ of gonorrhœa in connection with the material which has come under observation in the hospital, does not recall having met with reported cases of perichondritis, but there seems to be no reason why the complication should not occur.[1]

Bronzed Diabetes, with Enlargement of the Liver and Palpable Spleen. Dr. Barker.

The patient, J. W. S., a bricklayer, 53 years old, was admitted to Ward F on October 6, 1905, complaining of weakness and great thirst. He suffered from an attack of pneumonia in his seventeenth year. Chronic constipation has existed; otherwise he has been healthy and his habits have been good. His average weight is 160 pounds. We have inquired carefully, but can, in connection with the present illness, get no history of symptoms noticed by the patient dating farther back than three months. At about that time the patient noticed that he was growing weak in the legs. Six weeks ago he observed that he was passing large quantities of urine, urinating eight or ten times during the day, and three or four times during the night. The polyuria has been accompanied by excessive thirst and a voracious appetite, especially for sweets. During the past four weeks the patient has lost strength rapidly, and he states that he has diminished in weight by twenty pounds during the same period. He stopped work a week before admission.

The bronzing of the skin is, as you see, pronounced, especially on those parts of the body which have been exposed, though bronzing of a less degree affects the skin of the whole body. On the thorax the bronzing is mottled by small, paler areas, about 6 to 8 mm. in diameter. The openings of the sebaceous glands are very prominent. The patient states that he has always been of dark complexion, and he has not noticed that his skin is darker now than it was a year ago. Members

[1] Since the meeting at which this case was shown Dr. Sylvan Rosenheim has called my attention to three references bearing upon involvement of the larynx in gonorrhœa. These are all in Friedrich's Rhinology, Laryngology, and Otology in General Medicine. In two of the cases there were redness, swelling and fluctuation over the arytenoid cartilage, with loss of adduction of the vocal cord and aphonia; violent pain in the region of the larynx was complained of and was increased by pressure on the thyreoid cartilage. The third case referred to was one of bilateral paralysis of the M. crico-arytenoideus posterior, supposedly due to a neuritis of gonorrhœal origin.

of his family, however, state that they have noticed the increased darkening of the skin.

The patient is not anæmic. He has a normal number of white and red corpuscles, and 95 per cent of hæmoglobin in his blood. The urine shows a specific gravity of from 1034 to 1037. It is free from albumin, but contains a large quantity of sugar. An examination of a single specimen on entrance revealed the presence of 11.45 per cent of glucose. During the past twenty-four hours the patient has excreted 96.6 grams of glucose, an amount corresponding to 6.4 per cent of the urine. Acetone and diacetic acid are present in the urinary secretion to-day.

The patient's liver is very much enlarged, the superficial dulness extending in the right mammillary line from the sixth rib to a point 12.5 cm. below the costal margin. On palpation it is felt to be hard, and the surface is smooth. The enlargement involves the whole organ, including the left lobe. The edge of the spleen can be felt on deep inspiration in the left hypochondrium. In addition to the pigmentation there are extensive reddened areas of the skin on those parts of the body especially exposed to mechanical irritation; namely, in and about the axilla, above the breasts, at the waist band and between the thighs. This redness is in part a traumatic erythema, in part actually an eczema. Examination of the other organs is negative. The knee-jerks are present on both sides.

To-day Dr. Walter Jones, in the laboratory of physiological chemistry, made a spectroscopic examination of the fresh blood, but found only the normal bands of oxyhæmoglobin. The coagulation time is three and a quarter minutes. Blood pressure, 115 millimeters of mercury.

Regarding the diagnosis, it seems clear that we have to deal with a case of bronzed diabetes in association with hæmochromatosis, hypertrophic cirrhosis of the liver, and enlargement of the spleen. Doubtless chronic interstitial pancreatitis with enlargement also exists. The condition is an interesting one, and this is, I believe, the fifth instance met with in this hospital. Dr. Osler has reported several of the earlier cases.

It will be recalled that Dr. Opie some years ago showed the relation which exists between the so-called hæmochromatosis of von Recklinghausen, and the *diabète bronzé* of Hanot and Chauffard. It seems probable, from the studies of Opie, P. Marie, Anschütz, Buss, and others, that the diabetes is secondary to the hæmochromatosis. The conception of the disease held at present is as follows: For some reason as yet unknown two kinds of pigment accumulate in the body, the so-called hæmosiderin in the epithelial cells of the liver, pancreas and other glands, and the so-called hæmofuscin, in the smooth muscle of the alimentary tract, of the blood-vessels, of the genito-urinary tract, etc. As a result of the deposition of the hæmosiderin in the liver and pancreas the parenchymatous cells of these organs degenerate. This degeneration, together with the direct irritation of the pigment itself, acts as a stimulus to the growth of connective-tissue, and hypertrophic cirrhosis of the liver and chronic interstitial pancreatitis develop, the pancreas as a rule becoming half again as large as normal. When the chronic interstitial pancreatitis has reached a certain grade (according to Opie, when it has destroyed a sufficient number of the islands of Langerhans) diabetes develops. The diabetes is therefore a terminal phenomenon, and cases have been as a rule rapidly fatal after the diabetic symptoms have appeared. The hæmochromatosis, however, together with enlargement of the liver, may exist for many years without development of diabetes, and the case recorded by Dr. Opie never developed glycosuria. His patient died of typhoid fever.

In the ward rounds we have discussed in this case the possibilities of pathogenesis, with the hope of getting some clue which might enable us to reproduce the disease experimentally in animals, but the etiology and pathogenesis are far from clear.

In some instances of hæmochromatosis hæmorrhages into the peritoneal cavity or into the pleura or into the pericardium have existed, but these are not always present, and no evidence of such hæmorrhages can be found in the present case. Nor is there any evidence of increased blood destruction; the patient is not, nor has he been, anæmic. The accumulation of hæmosiderin,[2] assuming that it is derived from disintegrating red blood corpuscles, might occur conceivably from either one or two causes. Its accumulation might on the one hand be due to some abnormal cleavage of blood pigment. We know from laboratory studies that hæmoglobin may break up in different ways. It is possible that, in disease, cleavage may follow some route other than that normally travelled. On the other hand, it is possible that changes take place in the cells of the body, especially in the liver, which prevent the normal metabolism of the breaking down blood pigment, so that, though hæmoglobin cleavage may be regular as far as it goes, the cells may be unable to carry on the processes by which the cleavage products are normally utilized. It seems probable that some deep-lying disturbance of the iron metabolism is at the bottom of the affection, for the studies of Anschütz show that in this disease no less than 55 per cent of the ash of the liver consists of iron, an amount which is at least 100 times as great as the normal percentage.

Inversion of Uterus. Dr. Williams.

Case 1.—Woman, 24 years old; married two years; miscarriage at sixth month fifteen months before. In this instance patient went to term; labor was normal through first and second stages. The Credé method being ineffectual in removing the placenta, it was removed manually. The patient was very much shocked, but there was no hemorrhage. Twenty-four hours later Dr. Williams found her radials pulseless, heart rate 168, and the patient bathed in sweat. Palpation disclosed a firm hard mass in abdomen, and on vaginal examination the pelvic cavity was found filled with a large

[2] Unfortunately, "hæmosiderin" is as yet a mere histological term; it may or may not be a single chemical substance; it should be more thoroughly studied.

round mass with ragged edges. Above the tumor mass was the firm hard cervical ring through which the uterus had inverted. The ring was dilated manually, and the uterus being reverted promptly retracted and forced the hand out. The patient's condition improved rapidly, pulse was 100, and she was out of danger in a few hours.

Case 2.—Girl, 21 years of age; primipara delivered by forceps and placenta removed manually. When seen in consultation on the third day, her pulse was 140 and her uterus inverted, the cervix was hard, about the size of a dollar, and tightly gripped the inverted uterus. There was marked pressure on the bladder, which was greatly distended with bloody urine. Being unable to dilate the hard cervix, laparotomy was done, the cervix incised and with fingers in the vagina the uterus was reverted, the patient making a satisfactory recovery. Inversions of the uterus mostly occur in primiparæ attended by ignorant midwives, and are caused by traction on the cord or by too great pressure on the uterus from above.

Thoracic Aneurisms. Dr. Baetjer.

The X-ray has proven most useful in diagnosing conditions and diseases of the chest. We can now practically make positive and negative diagnoses. Both the radiographic and fluoroscopic methods are used in examination. The routine in this hospital is to make a physical examination, first to see that there are no abnormalities, then place the tube on a level with the third rib twenty-four inches from the patient's back and examine the chest from the front. The patient is turned around and examined in the same way from the back, and then sidewise by transverse illumination. In this way we cannot only get location of the aneurism but we can see whether or not it is pedicled. The normal fluorescent screen reveals the dark line of the spine and sternum about two inches wide, the shadows of the pulsating heart, and of the diaphragm. Any shadow to the right or left of the sternum is abnormal and may be due to enlarged glands, new growth, or aneurism. The shadow of a new growth is darker and more hazy than the shadow of the aneurism. Dilatation of the aorta is positive; when in pulsation the aorta disappears behind the sternum. To make a diagnosis of aneurism the shadow must persist between pulsations.

NOTES ON NEW BOOKS.

The Principles and Practice of Gynecology. By E. C. Dudley, A. M., M. D., Professor of Gynecology, Northwestern University Medical School. Fourth edition revised. (*Philadelphia: Lea Brothers & Co., 1904.*)

This edition is considerably larger than its predecessors. The introductory chapters give the reader a good idea of the normal functions of the pelvic organs and clearly outline the usual method of making pelvic examinations. The chapters on technique are detailed and explicit, and the section devoted to the preparatory and after treatment of patients is excellent.

The book is essentially a mirror of the methods employed by Dr. Dudley in his own clinic and little space is accorded the operations of other surgeons. This certainly increases the individuality of the work. The book is clearly written, the illustrations are good, and the type perfectly satisfactory. Taken as a whole the book is a safe clinical guide, notwithstanding the fact that its pathology is rather hazy and leaves much to be desired.

Addresses and Other Papers. By William Williams Keen, M. D., LL. D., F. R. C. S. (Hon.), Professor of Surgery, Jefferson Medical College, etc. (*Philadelphia and London: W. B. Saunders & Company, 1905.*)

This volume of addresses offers a wide range of subjects presented in a pleasing and interesting way. The historical and reminiscential papers seem upon the whole the most happy in matter and arrangement. They indicate a careful study of original sources of information and often, in fact, furnish history at first hand from the author's own experience. A good example may be found in the "History of the Philadelphia School of Anatomy and its Relation to Medical Teaching," with its charming personal sketches of Lawrance, Godman, Webster, Pancoast, Agnew, Da Costa, Brinton, and many others. The paper is enlivened by many touches of humor and several lively tales of early events in this pioneer school of anatomy. Another paper in the same vein and equally interesting is entitled "Surgical Reminiscences of the Civil War." We know of no more vivid picture of the surgical aspects of that memorable conflict. The deficiences and crudities of the medical and surgical service, the unpreparedness of the Army Medical Corps for the emergencies which had been thrust upon it, the lack of experience of many surgeons, the sufferings of the wounded, and the frightful mortality from surgical accidents, which we now know to be preventable, are graphically told.

Among the most exclusively professional papers may be mentioned "The Debt of the Public to the Medical Profession," "The Progress of Surgery in the Nineteenth Century," and "Medicine as a Career for Educated Men." These display high ideals of medicine and lofty hopes for its future, presented in a forceful and impressive manner.

In another vein may be mentioned a brief paper on the "Cheerfulness of Death," indicating a depth of religious feeling on the part of the author and a habit of mind, which are not common among medical men. The whole book is upon a high plane of thought and should have a wide circulation.

A Text-Book of Obstetrics. By Adam H. Wright, M. D., Professor of Obstetrics, University of Toronto. (*New York and London: D. Appleton and Company, 1905.*)

Dr. Wright is to be congratulated on the excellence of his book, which, apart from the first few sections dealing with anatomy and physiology, leaves little to be desired in the treatment of the subject; the author's apology in his preface is scarcely sufficient to excuse the brevity and lack of detail in this portion of the book.

The sections dealing with the management of pregnancy and labor are excellent, and it is interesting to note the importance laid upon pelvimetry. The section on the mechanism of labor is very brief. Probably the most interesting section in the book is that dealing with the intercurrent diseases of pregnancy. It is here that one gets an idea of the very wide extent of Dr. Wright's experience and his great capacity for clinical observation. In the section on eclampsia wise advise is given against the employment of useless drugs, but the treatment is not in accord with the usually accepted ideas. Indeed, here is one of the most

marked inconsistencies in the book, for, while immediate delivery of the patient, which offers the only possible chance of life for the child, is not considered advisable on account of the danger to the mother, in the treatment of postpartum hemorrhage, on the other hand, an expectant policy is advised on account of the child, even though the danger to the mother is considerably greater than it would be in eclampsia. The treatment of occipito-posterior positions is taken up somewhat extensively. The treatment advised is that in general use in the best maternities. Transverse presentations are rather scantily treated, and in the treatment of prolapsed cord the forceps is placed next to attempts at reposition, rather than version which would appear to give a better chance for the child. The sections on puerperal infection are full and complete. The treatment advised—purgation, water in large quantities, and stimulation, together with antistreptococcus serum—is most judicious. The sections on obstetrical operations are very complete. Dr. Wright believes in the waiting treatment rather than the immediate repair of extensive perineal tears. In the application of forceps he himself believes in the cephalic application, but he has described the pelvic application, which is the method in common use in England and in Canada.

The introduction of clinical histories of interesting cases, together with the forceful and personal style of Dr. Wright's diction, makes the book extremely interesting reading, and the excellent print and general get-up of the book commend it to the medical student as one of the most valuable of the numerous text-books on obstetrics which have recently appeared.

The Pharmacopœia of the United States of America. Eighth decennial revision. By authority of the United States Pharmacopœial Convention held at Washington, A. D. 1900. Revised by the Committee of Revision and published by the Board of Trustees. Official from September 1, 1905. (*Philadelphia: P. Blakiston's Son & Company.*)

At last the long expected new Pharmacopœia has been issued, and will be official from September 1, 1905. The former edition was known as the 1890 revision; the new work will be officially designated as the eighth decennial revision, the date 1900 forming no part of the title.

In the new book there are more important changes made in the strength of the preparations, more new products added, and more drugs standardized than ever before. Many synthetic articles, such as Trional and Urotropin have been admitted, but not under these names. It will almost be necessary for the physician to carry a pocket edition, for reference, when he wishes to prescribe these remedies by their pharmacopœial name. For instance: Trional is admitted as Sulphonethylmethane, Phenacetin as Acetophenitidin, Urotropin as Cystogen; and the many other names given the combination of formaldehyde and ammonia, as Hexamethylenamine.

J. L. W.

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CONTENTS.

PAGE

The Herter Lectures. Lecture II.—The Contributions of Pharmacology to Physiology. By Hans Meyer, ... 389

Cardiograms Obtained from a Case of Operative Defect in the Chest Wall. By Joseph Erlanger, ... 394

I. Fibroma of the Abdominal Wall; II. Primary Carcinoma of the Right Fallopian Tube; III. An Accessory and Twisted Omentum. By Dr. Thomas S. Cullen, ... 397

A Case of Sarcoma of the Eye, Involving Chiefly the Ciliary Body. By Paul G. Woolley, M. D., ... 402

Renal Decapsulation in Nephritis, with Report of a Case. By Henry Harris, M. D., ... 404

Dr. Charles Frederick Wiesenthal's Medical Reports. By Eugene F. Cordell, M. D., ... 407

PAGE

A Letter to the Graduates of the Johns Hopkins Medical School. By Dr. William Osler, ... 410

Proceedings of Societies:

The Johns Hopkins Hospital Medical Society, ... 411

Pulsating Empyema; Cystic Kidney [Dr. Cole];—Congenital Cystic Kidney [Dr. Bunting];—Infectious Arthritis [Dr. Fayerweather].

The Johns Hopkins Hospital Historical Club, ... 412

John Howard's Observations on Hospitals (1773–1790) [Dr. Hurd];—History of Typhoid Fever [Dr. McCrae].

Notes on New Books, ... 414

Index, ... 417

THE HERTER LECTURES.

LECTURE II.—THE CONTRIBUTIONS OF PHARMACOLOGY TO PHYSIOLOGY.[1]

By Hans Meyer,

Professor of Pharmacology in the University of Vienna.

Ladies and Gentlemen:

In my first lecture I touched upon a series of physiological problems that have been elucidated in a pharmacological way. I treated these problems in a merely cursory manner and did not enter upon details of the various investigations. Permit me to-day to discuss more fully a problem which has for a long time claimed my attention and which has for many years been a topic of research in my laboratory, namely, the problem of renal function.

As is well known, there are two leading and opposing theories on the nature of urinary secretion. According to one of these theories, which was developed most fully by Heidenhain, we have to deal with a true secretory process by which water and perhaps the salts pass through the glomerulus, whereas the specific constituents of the urine are liberated from the tubules so that the sum of both secretions is represented by the outflowing urine. According to the other hypothesis, which was first proposed by Ludwig and subsequently modified by his successors (in a biological sense), there goes on in the kidney side by side with the glomerular activity, dependent essentially on the mechanical conditions of the circulation, and independently also on the secretion of certain urinary constituents, a process of resorption in the urinary tubules. Through this resorption the slightly concentrated secretion of the glomerulus, corresponding to the water of the blood, undergoes concentration to a point characteristic of the urine.

The output of urine is chiefly conditioned on the largely physical excretory process, which, on account of its dependence on the blood flow, and the blood pressure in the kidneys, one is justified in regarding as a kind of filtration or transuda-

[1] Delivered at the Johns Hopkins Medical School, October 5, 1905.

tion. On the other hand, the resorption of water through the tubules is not directly dependent on the circulation of the blood. That is, it is in nowise proportional to the abundance of the glomerular filtration. It would be more nearly correct to say that this process is inversely proportional to the filtration. There is, therefore, the more abundant and unconcentrated urine when the blood flow is more abundant, and, on the contrary, a more scanty and concentrated urine when the blood flow is scanty.

The Ludwig theory, as you are aware, is based chiefly on the directly evident dependence of the urinary secretion on the blood stream through the kidneys and on the blood pressure, and in fact this connection is a striking one. I will remind you of the experiments of Goll which were conducted as long ago as the year 1854, in which the tension of the vessels was lowered by vagus irritation or by bleeding, or elevated by clamping the large vessels of the extremities, in which the volume of the urine rose and fell according to the increased or diminished flow of blood through the kidneys.

Against the whole theory of Ludwig, supported as it was by many other facts and arguments, Heidenhain brought a series of objections of which the following was especially impressive. If the human blood holds about one-tenth of one per cent of urea and if it be estimated that the daily excretion averages about 30 grams of urea, it would follow that on the smallest estimate 30 liters of fluid must filter through the kidneys in twenty-four hours, for which about 28 liters of water must be reabsorbed. But if, according to the calculation of Heidenhain, not more than 230 liters of blood pass through the kidneys in the course of a day, it follows that, according to Ludwig's view, about one-quarter of this volume filters out—a condition which would lead to a wholly impossible concentration of the blood in the glomerulus. In addition to this objection was urged the uneconomical work involved in the resorption through the urinary tubules of such great quantities of superfluous water. But we now know through the careful investigations of Tigerstedt that there flows through the kidneys during a very moderate diuresis in one minute a quantity of blood corresponding to 80 to 100 per cent of their weight, or, in other words, since the human kidneys weigh about 300 grams these organs are traversed by about 240 to 300 grams of blood in a minute, equivalent to 345 to 430 liters in twenty-four hours. Thus it is only about one-twelfth to one-fourteenth of the volume of blood, and not one-fourth of its volume, that is expressed. And so far as the chemical work of resorption is concerned, it must be remembered that the work of excreting 30 grams of urea through the elective action of the tubular epithelium from blood holding only 0.1 per cent of urea must be exactly as great as the corresponding work of resorption by the same cells—in order to concentrate a 0.1 per cent blood filtrate to 1.5 per cent of urea through the resorption of water. Now Heidenhain endeavored to demonstrate the specific secretory function of the epithelia by means of injection of coloring matters. He injected into the veins of a rabbit a definite quantity of sodium sulphindigotate and removed the kidneys after a certain period of time, injected the vessels with alcohol and examined the structures histologically. He then found under certain conditions that the glomeruli were wholly free from coloring matter; the epithelia of the tubules, on the other hand, were colored. And he concludes from this that the dye was not secreted from the glomerulus but was secreted by the tubules. And from these observations Heidenhain made the inference that the epithelia of the tubules secrete also other constituents of the urine.

These experiments are so well known that I do not need to enter more fully upon them; what concerns us here is that they secured a wide acceptance for the Heidenhain theory. But since the pharmacological study of glandular secretion as compared with renal activity has shown that these forms of cellular function are different and even opposed to one another in certain respects, and since the behavior of certain pharmacological agents is difficult to harmonize with the Heidenhain view and easier to bring into accord with the theory of Ludwig, a number of pharmacological studies have been undertaken with a view to testing the validity of the Ludwig theory. If, as Heidenhain maintained, the coloration of the kidney is an indication and measure of its normal secretory activity, it might be expected that by means of experimentally increased diuresis this coloration would show corresponding alterations, that is to say coloration would be intensified in the tubules. With this idea in mind Sobieranski, about ten years ago, began a new study of this subject in my laboratory by means of color injections carried out according to the Heidenhain method. His results on normal animals led him to the conclusion that dyes were not excreted by the convoluted tubules, as Heidenhain thought from his findings, but in company with the water stream through the glomeruli, whence the dye passed into the tubules and was absorbed into the epithelium, coloring their nuclei. Through the simultaneous reabsorption of water by the tubules, the dye-stuff solution becomes more and more concentrated so that it (the dye) under certain conditions is bound to be separated in a crystalline state in the epithelium.

This had already been shown to be the case by experiments with sodium sulphindigotate, but still more clearly by means of experiments with carmine, a dye which is better adapted to this kind of experimentation because it does not undergo reduction (with loss of color) in the tissues. Even more surprising and striking were the results obtained on diuresis under the influence of caffeine, sodium nitrate, or urea. Here the tubules were found to be very little or not at all colored. It was thus shown that an increase in the secretion of the dye through the tubular epithelium, which the hypothesis of Heidenhain calls for, under these circumstances did not exist. On the other hand, the process becomes intelligible through the explanation of Sobieranski. These diuretics give rise to diuresis by inhibiting the absorption of water from the urinary tubules, and at the same time prevent the absorption of the coloring matter by the tubular structures. Against this interpretation of Sobieranski's findings it is possible to offer

certain objections, the validity of which we have recognized from the beginning. The experiments of Sobieranski can be regarded as corroborative evidence of the resorption function of the urinary tubules, but not as positive proof of this function.

One may approach the subject, also, from an entirely different side. If the process of separating water from the blood in the glomeruli is not an elective secretory process, as in other glands, but is in reality a process analogous to filtration, that is to say is essentially dependent on physico-chemical conditions, then one would expect, as Tamman has already shown, that together with the free water of the blood (not held by the blood colloids) the dissolved crystalloid constituents, like urea and salts, would simultaneously filter through; in other words, that with increased separation of water these bodies would also be excreted in increased amounts. On the other hand, the colloids and other substances similarly held in the blood, which cannot transude or filter through the normal glomeruli, are not driven through with the water flow. They must rather be secreted through specific cell activity and quite independently of all mechanical filtration.

Indeed we have known for a long time from purely clinical observations that some urinary constituents, like urea and sodium chloride, are excreted almost proportionately to the volume of the urine; and that others, on the contrary, like uric acid and phosphoric acid, are not influenced by the quantity of urine. In order to examine this problem in a quantitative way, a series of observations have been made by my assistant and collaborator, Otto Loewi. These experiments were made on dogs and rabbits in the following manner: The normal excretion of uric acid, urea, and phosphoric acid was studied during a preliminary period of several hours. In still other cases the excretion of sugar was studied—indeed, not merely in diabetes following pancreas extirpation, but also after phlorhizin administration and intravenous injections of sugar. Then the secretion of urine was increased experimentally through free administration of water or by means of diuretics, such as sodium nitrate or caffeine, and during the diuresis so induced the above-mentioned constituents were quantitatively determined. Finally similar observations were made during and after the period following the cessation of the diuresis. The outcome was that the excretion of urea and of chlorides ran regularly parallel with the volume of the urine. On the other hand, there was never observed any parallelism between the excretion of water, on the one hand, and the increased amount of uric acid and phosphoric acid normally produced in the organism, on the other. I specially emphasize the phosphoric acid normally produced in the organism, for any phosphoric acid introduced as a salt into the circulation showed a different behavior. Such introduced salts followed the same law of excretion as the chloride and urea; and this general law held true in the case of sugar.

The blood, as is well known, always contains sugar, but in a combined form, so that the sugar under normal conditions is not excreted by the kidneys. But after pancreas extirpation or after an intravenous infusion of sugar in normal animals, the sugar content of the blood rises above the normal; the greater part of it cannot exist in combination in the blood but is free, and, like urea and other crystalloids, is excreted by the urine. And it appears from Loewi's experiments on diuresis that in such pancreatic or infusion diabetes, the quantity of excreted sugar was always proportional to the volume of urine excreted. In phlorhizin diabetes, on the other hand, the behavior was entirely different. As you are aware, there occurs no hyperglycæmia in phlorhizin glycosuria. There is no increase of free sugar in the blood, but the normally combined sugar is liberated from its combination and excreted from the kidneys. And this specific cellular sugar excretion was shown to be quite independent of the filtration of fluid through the glomeruli, that is, independent of the amount of diuresis. From this it seems to follow, in fact, that the substances which exist free in the blood pass out mechanically with the water; while other bodies, such as uric acid, phosphoric acid, phlorhizin-sugar, and probably the urinary pigments, are excreted from the kidney by special secretory activity. It is not necessary that a substance exist in a crystalline state in order that it be secreted by mechanical filtration through the glomeruli; it may equally well be a colloid; provided, however, that it is not combined with the blood tissue. It has long been known that dissolved hæmoglobin and injected albumin passed through the kidney into the urine. It is also shown by direct microscopical investigation that these bodies pass through the glomeruli. And, as in the case of urea and salts, this excretion of proteids through the glomeruli has been shown by experiments by Dr. Schmidt and Dr. Loewi in my laboratory to be a mechanical filtration.

This specific excretion of uric acid, etc., cannot be increased by any of the known diuretics. The action of diuretics, therefore, can surely not be explained by the supposition that there is a stimulation of the secretory activity of the kidneys. And, moreover, a specific renal secretion is something quite different from the secretory activity of the glands, for the typical glandular poisons, like pilocarpine, not merely are without influence on diuresis in general, but have no effect whatever on the specific excretion of uric acid, phosphoric acid, etc. If, then, the filtration of the watery constituents of the blood is highly probable, it follows that as a means of saving water there must be a compensatory resorption in the tubules analogous to the process of resorption from the alimentary canal. In the case of the intestinal tract large quantities of fluid are secreted from the mouth, stomach, and small intestines, even to the amount of several liters in twenty-four hours, which is later reabsorbed in the large intestine, especially in the colon, resulting in the semi-solid fæces. And a similar process may be conceived to go on in the kidneys.

We have undertaken to determine whether this conception is correct. If under normal conditions such a process of concentration occurs in the tubules, one would expect a diarrhœa (that is, a flow of unconcentrated fluid from the blood)

to result from elimination of or injury to these parts; just as there results a flow of watery fæces if the colon be removed or its cells paralyzed by poisons, or if the contents of the intestines are rendered incapable of absorption by the addition of certain salts. With this thought in mind, Ribbert long ago conducted experiments involving the removing of the medulla of the kidney, as a result of which he did, in fact, observe an increased secretion of a very dilute urine in rabbits. Similar experiments were undertaken by Dr. Hausmann and myself three years ago, by means of a somewhat modified operative technique and especially with the aid of quantitative analysis of the urine. In rabbits from which the right kidney had been removed previous to operation on the left kidney, we found the excretion of urine increased three or four times, just as did Ribbert, and observed a change from a concentrated mucous-like urine before the operation to a light-colored watery urine of low specific gravity after the operation. Quantitative analysis further gave the noteworthy result that whatever might be the normal content of chlorides and urea, after the operation, the content always approximated that of the blood serum; for example, if the normal content of the sodium chloride in a diet poor in this salt averaged 0.1 per cent, or in a diet rich in sodium chloride approximated 2 to 5 per cent, after the operation there would result in each case a percentage of sodium chloride which varied within the narrow limits of 0.6 to 0.8 per cent. This result seemed to speak strongly for the resorption theory. The resorption activity of the kidney may be influenced by pharmacological means as well as by removal of the uriniferous tubules. One would expect, as in the case of the intestines, that salts would check resorption from the tubules, and, further, that as in the case of the intestines, the bibasic would act more strongly than the monobasic salts. Comparative study of the action of Glauber salt and common salt injected into the blood vessels, made by Dr. Halsey, yielded the expected results. Results similar to these unpublished ones have been obtained by Gottlieb and Magnus, of Heidelberg, and especially by Cushny, of Ann Arbor. The isosmotic solution of Glauber salts possessed a much more strongly diuretic action than common salt. From these experiments we may conclude with Cushny that the salts prevent water resorption from the tubules and set up a kind of diarrhœa in proportion to their power of withdrawing water, and that hence, in accordance with the Ludwig theory, we must assume that a resorption of water occurs under normal conditions. The matter is, however, not quite so simple, for the salts, owing to their ability to withdraw water, also withdraw water from the tissues into the blood, thereby increasing the filtration stream through the glomeruli. Cushny further showed that fixed constituents, like sodium chloride, may be reabsorbed, as in the case of the intestines, by the epithelia of the tubules, that the difficultly diffusible Glauber salt was only slightly and slowly reabsorbed, and that finally urea is apparently not reabsorbed at all. A further striking example of such a renal diarrhœa, as I am inclined to call it, has been brought forward by Loewi. As I have already stated, every diuresis dependent on increased glomerulus filtration, occasions also an increased excretion of sodium chloride and urea. If one poisons an animal with phlorhizin, there also occurs an increased diuresis. This phlorhizin diuresis, as Brodie showed, appears to be wholly independent, in general, of the circulation and especially of the circulation through the kidney. And, what particularly interests us here, this diuresis is not dependent on the filtration of water through the glomeruli, for, according to Loewi's analysis, the chlorides and urea were not excreted in increased amount as is the case in all the other forms of diuresis. The phlorhizin diuresis must be regarded therefore as a pure tubular diarrhœa, brought about by the sugar excreted in the tubules of the kidney itself and there hindering the reabsorption of water by means of its water attracting properties.

We have, therefore, in many instances two closely connected processes which constitute the basis of increased diuresis: the interference with resorption from the tubules, and the increased filtration through the glomeruli, the latter being probably the more important factor. The question arises, What are the conditions that determine the operation of these factors? It may be that to a slight extent the diminished viscosity of the blood or, more properly, the degree of saturation of the colloids of the blood with water, are here concerned. We know that in thirsting animals the kidney secretion cannot be increased in any way; we have, therefore, no quantitative conception of the extent of this influence. On the other hand we know of one factor which is of determining significance for the process of filtration. This is the blood flow through the kidney. It was long ago shown by Roy that as a rule every diuresis is associated with an increase in the volume of the kidney, that is, sets in simultaneously with an increased blood flow, and the experiments of Roy have been repeatedly carried out with essentially the same results by numerous investigators, and especially by Gottlieb and Magnus and by Starling and Bayliss. Still it appeared from time to time that there were exceptions in which increased diuresis occurred in association with an unchanged volume or scarcely perceptible increase in the volume of the kidney. Gottlieb and Magnus, therefore, felt justified in concluding that the increased blood flow through the kidney is not the primary and determining condition for increased diuresis, but rather a regular and not essential associated phenomenon. My collaborator, Professor Loewi, also carried on a large number of experiments in this direction. He too found that in certain cases the oncometer showed no increase in the volume of the kidney, notwithstanding an increase in diuresis. We further undertook to determine whether diuresis occurred under the influence of diuretic agents like caffeine and salts even when the volume of the kidney was fixed so that an increased blood flow is presumably prevented. For this purpose the left kidney of the rabbit in a relatively quiescent and relatively anæmic condition was encased in plaster of paris with the exception of the hilus only, so that an increase in the volume of the kidney was wholly excluded. The surpris-

ing result was obtained that even in the case of such rigidly enclosed kidneys diuretics like caffeine and salts were able to induce an abundant diuresis. Hence it seemed to be actually true that an increased filtration may be induced without any increase in the blood flow through the kidneys. But more careful investigations showed that the volume of the kidney is by no means a certain measure of the blood flow through this organ, but that the volume of the kidney and the blood flow through it may be independent. For by inspection of the outflowing venous blood it could be seen that, notwithstanding the rigid limitation in the volume of the kidney, the flow of blood through the organ was always enhanced during diuresis. While the blood which flowed through the renal vein was dark previous to the diuresis, the stream took on a light, arterial color under the influence of caffeine and salts. The mere fact, therefore, that the kidney does not increase in size in some cases of caffeine diuresis is no proof that the process of diuresis does not depend on an increased flow of blood through the kidney, and one may say that an increased renal blood flow is a regular and essential condition of diuresis from salts, urea, and caffeine, a condition wholly sufficient, in itself, to explain the diuresis. It is not possible to say with certainty whether in the case of caffeine diuresis there is also a diminished resorption of fluid through the urinary tubules, as Sobieranski's experiments appeared to show. Another important fact was brought out by Loewi in this connection; we know that every hydræmia, whether induced by the administration of water or by the withdrawal of water from the tissues by means of salts intravenously injected. gives rise to an increased diuresis, without any increase in the general blood pressure or the work of the heart. What is the origin of such a diuresis? Loewi found that every hydræmia, whatever may be its origin, acts upon the vessels of the kidney as a specific excitant, in that it dilates the vessels and thus causes an increased glomerular filtration. Thus we have obtained an explanation for the increased secretion of urine arising from all forms of hydræmia, from the drinking of water, and from the withdrawal of water from the tissues, in consequence of the action of the diuretic salts. Hence we may say that all the observations that have come to us by physiological and pharmacological methods harmonize with the conception that the water of the blood and the free crystalloids therein dissolved are liberated from the glomeruli by the process of filtration or perhaps a process better described as transudation, and further that the urinary tubules reabsorb, by means of their epithelial cells, not only water but also, in cases of salt poverty, sodium chloride as well (these being materials which the organism cannot afford to lose), while at the same time these epithelial cells, like those of the intestines, have also to perform the duty of excreting the combined substances of the blood by means of their specific secretory activity.

Diuresis, therefore, represents the fusion of two principal processes—one concerning the glomeruli, which is in its main features mechanical in its nature; the other pertaining to the urinary tubules, which is not yet explicable on any physico-chemical hypothesis. The process of resorption from the urinary tubules has a distinctly biological, that is teleological character; water and salt are only reabsorbed when the organism does not possess these in excess. If one administers an abundance of water, the urine acquires a highly watery character, while after the administration of an abundance of sodium chloride there is a failure on the part of the tubules to reabsorb salt, as Loewi has shown. The process of reabsorption adapts itself, therefore, to the requirements of the organism.

Although I believe that the theory of renal function which I have here presented is the one which has the best experimental foundation, I readily concede that it leaves many facts still unexplained. For example, it is difficult by means of this hypothesis to explain the constitution of the urine in diabetes insipidus as well as the complete retention of chlorine under certain conditions, and I fancy that we shall have to suppose, as Cushny has done, that there is some kind of combination of sodium chloride with the blood tissue which hinders its filtration. The theory of diuresis and the action of diuretic drugs further possesses a practical interest. If, for example, it be true that caffeine acts diuretically through local specific dilation and not through irritation of the secretory cells, as was formerly supposed, then, as Loewi thinks, we are justified in its administration during long periods in the course of nephritis in which, in many instances, the vessels of the kidneys are abnormally contracted. And there is some reason to believe that the vasodilator action of the caffeine not merely induces an increased diuresis but exerts a favorable influence upon the pathological condition of the kidney itself.

In conclusion, I desire to express my appreciation of the courteous attention you have accorded me.

STUDIES IN TYPHOID FEVER.

SERIES I-II-III.

The papers on Typhoid Fever, edited by Professor William Osler, M. D., and printed in Volumes IV, V and VIII of the Johns Hopkins Hospital Reports, have been brought together and bound in cloth.

The volume includes thirty-five papers by Doctors Osler, Thayer, Hewetson, Blumer, Flexner, Reed, Parsons, Finney, Cushing, Lyon, Mitchell, Hamburger, Dobbin, Camac, Gwyn, Emerson and Young. It contains 776 pages, large octavo, with illustrations.

The price is $5.00 per copy. Address The Johns Hopkins Press, Baltimore, Maryland.

CARDIOGRAMS OBTAINED FROM A CASE OF OPERATIVE DEFECT IN THE CHEST WALL.

By Joseph Erlanger.

(From the Physiological Laboratory of the Johns Hopkins University.)

Historical Introduction.

Since the publication by Chauveau and Marey, in 1863, of the pioneer comparisons of the movements of the heart with the changes of the intracardiac pressure, cardiographic investigations on human beings have become almost a routine in the physiological laboratory and at the bedside. But despite the great amount of work that has been done we are still far from having a satisfactory knowledge of the form of the normal cardiogram and there is still much to be learned of the relation which the various features on the cardiogram bear to the events of the cardiac cycle.[1] The greatest difficulty in the way of the solution of these problems consists in the rigidity of the chest wall which lies between the heart and the receiving instruments. By it not only is the form of the cardiogram modified, but also the time relations of some of the features of the cardiac cycle may be altered. In order that data may be obtained which may serve as a means of interpreting the human cardiogram it is essential, wherever possible, to obtain tracings of the movements of the heart in all cases in which, for one reason or another, it is more or less freely exposed.

The number of satisfactory cardiograms that have been obtained from such cases of *ectopia cordis* is very small indeed. François-Franck[2] seems to have been the first investigator to have studied graphically the movements of the more or less freely exposed human heart. In 1877 he obtained beautiful and satisfactory tracings from a case in which a developmental defect permitted the heart to present in the sack of a ventral hernia. Some years later, in 1889, the same author had the opportunity of confirming his results in another exactly similar case.[3]

In 1879, Gibson and Malet[4] published tracings obtained from a pulsating tumor which presented in a congenital fissure of the sternum. These authors were unable to determine what part of the heart composed the tumor. Their waves seem to be made up of a combination of auricular and ventricular movements.

In 1882, v. Ziemssen[5] made a careful study of the movements of all of the chambers of the heart, excepting the right auricle, in a case in which the pericardium had been exposed as a result of the removal of a tumor of the chest wall. This case had been previously investigated by Grützner and by Filehne and Penzoldt.[6]

Macdonnell[7] studied the movements of the heart in a case with such lax abdominal walls that the hand carrying the receiving instrument could be inserted behind the heart. In this way he obtained tracings from the auricles and ventricles at different times. It is obvious that this method of obtaining tracings is much too uncertain to yield satisfactory results.

In 1898, tracings were obtained by Jarotzky[8] from the ventricles of a heart exposed by an operative defect in the chest wall and pericardium. It seems that the receiving instrument was held in the hand. At all events, the tracings that Jarotzky obtained are very irregular and, furthermore, his drum revolved so slowly that it is impossible to study the finer details of the curves.

Finally, we wish to refer to a case of *fissura sterni* which has recently been carefully investigated by Jaquet and Metzner.[9] This case was first studied by Jahn,[10] who made no tracings, and later by Penzoldt[11] and by Deuticke.[12] There seems to have been some difficulty in determining the identity of the parts of the circulatory system which presented in the fissure. Jahn and Penzoldt thought that the main pulsating tumor was the aorta, whereas Jaquet and Metzner and Deuticke believe it was the right ventricle. Jaquet and Metzner and Criegern[13] think that their X-ray examinations of the case support the latter view; but it should be stated that the X-ray examination made by Sternberg[14] at about the same time confirms the older view, namely, that the main pulsating tumor was the aorta.

Description of the Case.

The author has recently had the opportunity of studying the movements of the heart in a patient who had had a large part of the ribs on the right side of the chest removed for

[1] The literature on the normal cardiogram and a valuable discussion of the shortcomings of our knowledge of it will be found in an article by Tigerstedt: Ergebnisse der Physiologie, 1902, I, pt. II, p. 234.

[2] François-Franck: Trav. d. lab. d. Marey, 1877, III, p. 317.

[3] François-Franck: Arch. d. physiol. norm. et path., 1889, Ser. 5, I, p. 70.

[4] Gibson and Malet: Jr. of Anat. and Physiol., 1879-80, XIV, p. 1.

[5] v. Ziemssen: Deut. Arch. f. klin. Med., 1882, XXX, p. 277.

[6] Referred to by v. Ziemssen, l. c.

[7] Macdonnell: Practitioner, 1890, XLIV, p. 178.

[8] Jarotzky: Zt. f. klin. Med., 1898, XXXV, p. 301.

[9] Jacquet and Metzner: Deut. Arch. f. klin. Med., 1901, LXX, p. 57.

[10] Jahn: Deut. Arch. f. klin. Med., 1875, XVI, p. 200.

[11] Penzoldt: Deut. Arch. f. klin. Med., 1879, XXIV, p. 513.

[12] Deuticke: Ref. Jaquet and Metzner, l. c.

[13] Criegern: Münch. med. Wochenschr., Oct. 2, 1900.

[14] Sternberg: Verh. der physiol. Ges. zu Berl., Feb. 23, 1900, Arch. f. Physiol., 1900.

the treatment of empyema.[15] (See Fig. 1, which is a reproduction of a photograph of the patient.) Percussion indicated that the heart was but little displaced, and this is confirmed by a radiogram for which, together with some notes on the history of the case and the privilege of examining his tracings, the author is indebted to Dr. Yandell Henderson of New Haven. Owing to the emaciated condition of the patient the heart was covered laterally by but a thin layer of tissue—skin, mainly. Therefore, upon inspection it was almost possible to make out the form of the heart by the bulging which it caused of the thin layer of tissue overlying it. (See Fig. 1.) There could be seen a broad pulsating area extending from the prolongation of the upper border of the fifth rib to about the middle of the prolongation of the third interspace and between the anterior axillary line and the line formed by the projecting stumps of the amputated ribs anteriorly. Above this, about in the line of the third rib, there could be seen another more limited pulsating area. Palpation—it was almost possible to grasp the two regions of the heart—and the radiogram indicate that these pulsating areas were formed by the ventricles and auricles; and the cardiograms leave no room for doubting this conclusion. Furthermore, the fact that the position of the heart seemed to be but little altered from the normal, makes it appear more than probable that the lower and upper pulsations were produced by the left ventricle and auricle respectively.

Methods.

The tracings were made with Marey's cardiograph. The *pelotes* were placed over the lowermost point of the lower pulsating area (over the cross in Fig. 1) and over the middle point of the upper pulsating area. The receiving instruments were rested on the patient's chest. In order to bridge over the flaccid part of the chest wall the supports of the instruments were greatly prolonged by soldering to them long, stiff, metal strips. For the most part simultaneous tracings were made of the upper and lower pulsating areas together with the time in fifths of seconds. In some experiments these were combined with a tracing of the brachial pulse made with the sphygmomanometer devised by the author, and of the time in fiftieths of seconds.

All of the many tracings obtained have essentially the same form. Three of them, each illustrating slightly different features, are here accurately reproduced (Figs. 2, 3, and 4). The upper and lower (or middle) tracings will be designated the auricular and ventricular cardiograms respectively. In Fig. 3 the lowest tracing is the brachial sphygmogram.

Description and Discussion of the Tracings.

In the ventricular cardiogram (Fig. 2) the line, 4-5, is undoubtedly produced by the contraction of the auricles. In time it corresponds accurately with e-f, which must, therefore, represent the diminution in the volume of the auricles during their contraction.[16] The volume of the auricles then immediately increases even before the ventricles begin to contract. This is probably due largely to relaxation of the auricles and possibly, in part, to a reflux of blood from the ventricles, plus bulging of the auriculo-ventricular diaphragm. This increase of the auricular volume continues through a large part of the period of rising tension of the ventricles, 6-7 (see below), and is probably caused by further bulging of the auriculo-ventricular diaphragm and by filling of the auricles from the veins. But the auricular volume begins to diminish (beginning 7-8-h) toward the end of the period represented by the line, 6-7, and the diminution continues for some time thereafter. This diminution in the volume of the auricles, or rather the negative wave occurring at this time, has been variously explained.[17] According to Porter[18] it is caused by a descent of the auriculo-ventricular diaphragm resulting from contraction of the papillary muscles. Mosso believes it is caused by an increase in the negativity of the intrathoracic pressure caused by the diminution in the volume of the ventricles. Whereas François-Franck attributes it to relaxation of the auricles. In our case, as well as in the case of François-Franck, the second explanation given above cannot be held; the chest wall was so lax that the diminution of the volume of the ventricles could not have altered the intrathoracic pressure materially. Neither is it necessary to assume that contraction of the papillary muscles causes this negative wave, because it may be seen in the veins in cases of heart-block where the contraction of the auricles may not be followed by contraction of the ventricles.[19]

The cause of the descent, 7-8, in the ventricular cardiogram is not clear, unless it is due to a movement of translation of the whole heart. It was at first thought that it might have been caused by the diminution of the volume of the ventricles which occurs after the opening of the semilunar valves. But it may be seen in Fig. 3 that the aortic valves open presumably at some point near the foot of this descending line; for when the correction is made for the time lost in transmission of the pulse-wave to the brachial artery,[20] the arterial pulse

[15] The thanks of the author are due to Dr. Thomas R. Brown for calling his attention to this case.

[16] As is well known, the form of the cardiogram is determined by a combination of volume and pressure effects, and the form of curve obtained depends to a certain extent upon the pressure exerted on the heart by the receiving instrument. As this pressure cannot be nicely controlled it becomes practically impossible to distinguish pressure from volume changes. For the sake of convenience we shall usually refer to changes of tension in the tambour system and of the movements of the lever corresponding therewith as volume changes of the heart.

[17] Most of the literature on this subject will be found in Gerhardt: Schmied. Arch., 1894, XXXIV, p. 402.

[18] Porter: Jr. of Physiol., 1892, XIII, p. 513.

[19] Erlanger: Am. Jr. of Physiol., 1905, XIII, p. xxvi.

[20] The rate of transmission of the pulse-wave in the brachio-radial artery of this case was 6.8 meters per second. The distance of the place on the arm from which the sphygmogram was obtained was approximately 35 cm. The delay would, therefore, be approximately equal to 1.8 divisions on the time record.

begins at a point marked x on the ventricular cardiogram. Indeed, it seems to correspond with, or, perhaps, to come a trifle earlier than, the break in the curve at this place. But be that as it may, it is obvious that the period of rising tension extends from 6 to, at least, x.

The plateau stage of ventricular contraction now follows. On the declining plateau, which extends from 8 to a point beyond 11, there may be seen two distinct undulations with their crests at 9 and 11. Shortly before the beginning of this stage of ventricular contraction, the volume of the auricles begins to increase, the increase, h-m, outlasting slightly the plateau stage of ventricular contraction. Between h and m there may be seen three undulations, two of which, h-j and j-l, correspond in time with, and have the same sign as, the undulations 8-10 and 10-11 + on the ventricular cardiogram. It seems improbable that these waves are the result of instrumental error because the two recording instruments, while executing different motions, record the same waves. These waves have been frequently seen on intraventricular pressure curves and cardiograms obtained from animals,[21] and they are present on the human cardiogram made by François-Franck. Marey attributes them to waves in the heart generated by movements of the column of blood in the arteries, whereas Fredericq thinks these undulations are caused by the contraction of the heart muscle in three stages. By some they are believed to be artefacts of unsatisfactory instruments.

Ventricular relaxation begins at some point beyond 11, probably at l, and extends to 12. At the point marked l, a slight indentation may be seen in both the auricular and ventricular curves. It is indistinct in Fig. 2 because here the wave, 11, passes almost indistinguishably into the line which marks ventricular relaxation. But in Fig. 3, where the excursion of the lever was less than in Fig. 2, there can be no doubt but that ventricular relaxation begins at l. The volume of the auricles begins to diminish at the point marked m on the ventricular cardiogram. This point, therefore, indicates accurately the position at which the pressure in the ventricles falls below the intra-auricular pressure, *i. e.*, it marks the moment of opening of the auriculo-ventricular valves. It is interesting to note that this event is associated with no obvious sign on the ventricular cardiogram. But it should be stated here that in ventricular cardiograms obtained from animals, a small wave is often seen on the curve in just about the position at which, in our tracings, the auriculo-ventricular valves open. And Fredericq believes that this wave is caused by the flow of blood from the auricles into the ventricles when these valves open.

The auricular volume continues to diminish (latter part of m-n) for a short while after the completion of ventricular relaxation (after 12). During this period the volume of the ventricles increases very rapidly, 12-2. Possibly this is due to the pouring into the ventricles of the blood which has accumulated in the auricles during the period of closure of the auriculo-ventricular valves. The auricular volume then increases, rapidly at first, b-c, but soon the curve reaches the summit of a more or less horizontal plateau, c-e. On this plateau there are, at c and e, two gentle undulations. During this phase of the cycle the ventricular volume increases very slowly, 2-4, and this curve likewise shows two undulations which correspond more or less accurately with c and e. The origin of these waves is not known, but it seems possible that the wave e which immediately precedes the auricular contraction might be caused by contraction of the great veins or by a slowly beginning auricular contraction.

In Fig. 3 it may be seen that the dicrotic notch of the arterial pulse-wave corresponds in time with about the middle point of the line, 11-12, which represents ventricular relaxation. The ventricular curve is not affected by it.

It should be mentioned that these tracings do not show the intersystole described by Fredericq in cardiograms obtained from animals, and pictured by Jaquet and Metzner in a cardiogram obtained from man.

TABLE GIVING THE TIME RELATIONS OF THE VARIOUS FEATURES ON THE TRACINGS OF FIGS. 2, 3 AND 4.

No. of cardiac cycle	Duration of A systole c-f	Duration of Av-Vs interval 4-6	Duration of period of retardation 6-8 (?)	Duration of V plateau 8 (?)-11 (?)	Duration of V relaxation 11 (?)-12	Duration of heart pause 12-4	Duration of cardiac cycle 1-12	
4	.06	.14	.12 +	.32	.04 +	.34 +	1.	Fig. 2
5	.06	.14 +	.12)	.32	.06	.6 −	1.06	Fig. 2
6	—	.12 +	.12 +	.32	.06	—	—	Fig. 2
2	.07	.12	.12)	.27	.06	.36	.9	Fig. 3
3	.1 −	.08	.18	.22	.06	.16	.78	Fig. 4
4	.06 +	.1	.16	.24	.06	.16	.76	Fig. 4
5	.1 (?)	.14	.16	.24	.06	.24	.84	Fig. 4
6	.1	.14	.16	.24	.06	.32	.90	Fig. 4
7	.1	.14	.16	.24	.08	.36	.98	Fig. 4
8	.08	.12	.16 −	.26	.06	.42	1.02	Fig. 4

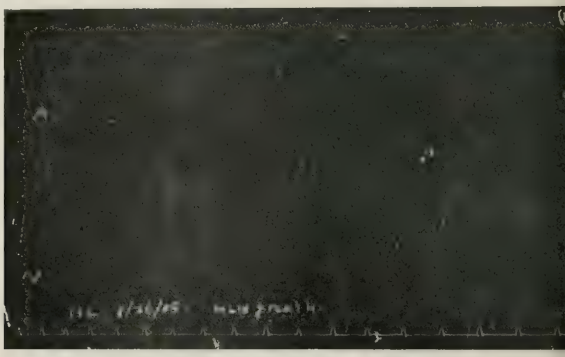
Attention should be called to the relation on the ventricular cardiogram of the curve of auricular contraction to that of ventricular contraction. In most of the tracings there is a distinct notch between these two features. But it may be seen that in the early parts of Fig. 4 the two waves are almost merged into a single, unbroken, ascending line. This is somewhat exaggerated in the figure because in the earlier portions of the tracing the drum was revolving more slowly than later. But accurate measurement shows that the interval between the beginnings of auricular and ventricular contractions were increasing while the tracing was being made. It is, therefore, obvious that under certain circumstances the two curves might actually be indistinguishably merged. In such a case it would be impossible to determine from a study of the ventricular cardiogram alone the moment of the beginning of ventricular contraction.

It may also be seen that in Fig. 4 the length of the phase

[21] See Tigerstedt, l. c.



FIG. 1.



F



F

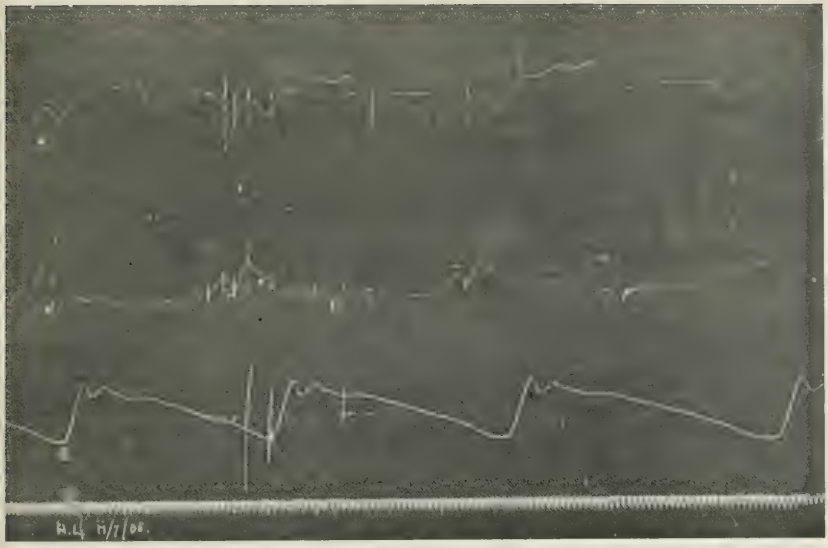
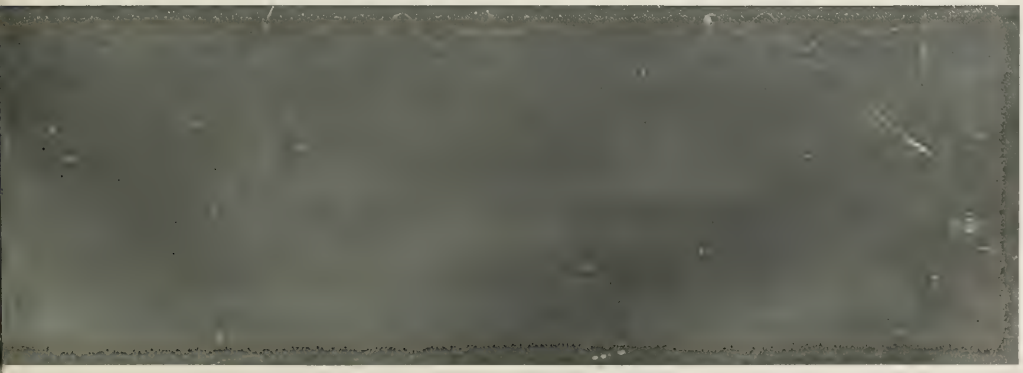


FIG. 3.





of the cycle which corresponds with the interval, b-e, of Fig. 2 was rapidly increasing while the tracing was being made. This phase corresponds with the so-called heart-pause—no active movements of the auricles or ventricles occur at this time; it is the phase of the cardiac cycle which is most affected by variations in the heart-rate. Inspection of the table will show that here the heart-rate was rapidly diminishing and that, although practically all of the phases of the cycle were correspondingly lengthened, it is the heart-pause which was most markedly affected.

In the table on the preceding page are given the analyses of the curves used to illustrate this article.

I. FIBROMA OF THE ABDOMINAL WALL; II. PRIMARY CARCINOMA OF THE RIGHT FALLOPIAN TUBE; III. AN ACCESSORY AND TWISTED OMENTUM.[1]

DETAILED DESCRIPTION OF CASES REPORTED BEFORE THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY, APRIL 3, 1905, BY DR. CULLEN.

I. Fibroma of the abdominal wall springing from the sheath of the external oblique (Fig. 1).

Mrs. H. M., 30 years old, was referred to me by Dr. Howard Bratton, of Elkton, Md., on Feb. 5, 1905. About three years ago she noticed a very small lump in the left side just beneath the ribs. This increased slightly in size for over two years, but during the last few months has grown rapidly. She thinks she is losing some in weight. On examination a kidney-shaped mass was found just below the free margin of the rib and on a line with the nipple on the left side. It was fairly movable and seemed to be just beneath the skin. On making an incision over it we found that the growth sprang from the sheath of the abdominal muscles, and lay between the muscle and adipose tissue. It was 13 cm. in length and varied from 8 to 10 cm. in breadth. It was lobulated and on its outer margin had a deep hollow that might readily be mistaken for the pelvis of the kidney.

Pathological Examination (Gyn.-Path. No. 8290).—The growth varies from 4 to 6 cm. in thickness. In some places it is covered by fat, but on the under surface over a wide area it is intimately blended with the muscle (Fig. 1). It is exceedingly hard and on section bears a striking resemblance to a fibroma. There is a definite and somewhat globular nodule forming about half of the tumor. This portion is somewhat homogeneous, is slightly yellowish in color, and at first suggests the possibility of sarcoma.

On histological examination the growth proved to be a typical fibroma. The nuclei were oval, spindle-shaped or irregular, and stained fairly deeply. The blood supply seemed abundant. We failed to find any areas suggestive of malignancy.

II. Primary carcinoma of the right Fallopian tube (Fig. 2) *with secondary involvement of the uterus, both ovaries, pelvic peritoneum, omentum, and rectum. Removal of omentum, uterus and appendages, one-third of the pelvic peritoneum, and six inches of the bowel. The patient was comfortable and considered herself well, five months after operation. The respite was, of course, only temporary.*

Mrs. Z. was seen in consultation with Dr. J. Milton Linthicum, Jan. 5, 1905. The patient was 55 years of age. She was sparely built, fairly well nourished, but slightly anæmic. For months she had had some hemorrhage from the uterus and later great pain on defecation; in fact her discomfort had been so great that she said she could not endure it much longer. On examination, under anæsthesia, I found the uterus slightly enlarged and on the right side a firm mass about 6 cm. in diameter. I thought it to be a myoma.

Jan. 7.—On opening the abdomen I found the omentum everywhere studded with nodules, some of them being very small, others 1 cm. or more in diameter, and umbilicated. I questioned the advisability of operating, but Dr. Linthicum thought it wiser to operate, as the patient said "she would rather die than go through the torture that she had been experiencing for several weeks." The omentum was separated close to the transverse colon, as in the vicinity of the colon no metastases were to be found. The right tube was much enlarged and apparently involved in a malignant growth. It was attached to the pelvic floor and the peritoneum at this point, over an area fully 5 by 6 cm., was involved in the process. On the right side the ureter ran directly beneath the thickened peritoneum. On the left side the ovary, although small, was glued down to the pelvic floor directly over the ureter. Posteriorly the uterus was firmly attached to the rectum. It was found necessary to carefully dissect out the ureters first, as it was evident that much of the pelvic peritoneum must be removed. The hysterectomy was carried out practically along the lines laid down by Wertheim's operation. Fully one-third of the pelvic peritoneum, however, was removed. I had hoped to remove part of the rectum with the uterus in one piece, but found that it was impossible. Consequently it was necessary to separate the uterus from the rectal growth. The rectum was freed on all sides, care being taken, however, not to interfere with the blood supply. The patient was then placed in the perineal position and the skin

[1] A brief report of these cases appeared in the BULLETIN for June, 1905, p. 237.

separated from the rectal mucosa, just as is done in a Whitehead operation. Six inches of the rectum were drawn down through the sphincter and cut off and the upper edge of the rectum was sutured to the skin. The ureters were covered over as far as possible with the remaining peritoneum. A medium-sized gauze drain was introduced into the pelvis and brought out through the vagina. The entire operation took a little more than three hours. The patient had a very feeble pulse when she left the table, which was not surprising, as she was in a weak condition at the commencement of the operation.

Jan. 8.—The patient is improving greatly. Her pulse is 126, temperature normal, respirations about 30. This evening there has been considerable vomiting. Sixteen ounces of water were ordered with the hope of washing the stomach out. She vomited four ounces, fortunately retaining the twelve. There have only been about 70 cc. of urine in twenty-four hours, but the general condition does not seem to indicate any uremia.

Feb. 1.—The patient has steadily improved since operation. There has been a great deal of discharge from the pelvis, but that is rapidly diminishing. She occasionally has a temperature of 101° F. The sphincter action at first was rather tardy, but is now much better.

March 1.—The patient is up and around and suffering little or no discomfort. Of course, a complete recovery is out of the question. The operation was performed merely to relieve her intense suffering.

Subsequent history.—During the spring and part of the summer she was free from pain, journeyed to distant points, and looked very well. About the middle of August she became rather weak; after seven days' rest in bed she suddenly grew worse and died in half an hour. From the symptoms it is possible that death was due to embolism. The operation relieved her of great suffering and gave her over six months of comparative comfort.

Gyn.-Path. No. 8114. The specimen comprises the uterus and enlarged right tube, both ovaries, the small left tube, and a cuff of pelvic peritoneum, the greater part of the omentum, and several inches of the rectum.

The uterus has been removed entirely. It is 7 by 5 by 3.5 cm. and is covered by numerous adhesions. The uterine cavity is of the normal size. The mucosa is thinner than usual and shows nothing of interest.

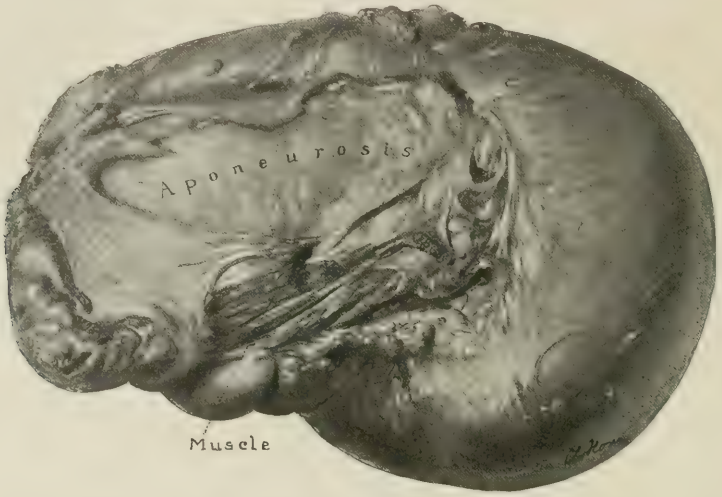


Fig. 1.—Fibroma Springing from the Aponeurosis of the External Oblique, and Lying Between the Muscle and the Skin.

The under or posterior surface of the tumor is shown. The growth bears some resemblance to a kidney in its general contour; on its lower surface is a depression which on palpation might readily be mistaken for the renal hilum. Attached to the tumor is some muscle, also a moderate amount of fat.

The right tube at the uterus is 3 mm. in diameter. After passing outward 1.5 cm. it suddenly increases in size, reaching a diameter of 1.8 cm. It gradually increases until near the fimbriated extremity it is 4 cm. in diameter. The entire length of the tube is approximately 12 cm. It is for the most part smooth, but at two points on its inner aspect the muscular coats have given way and we have hernial spaces .8 by 1.8 cm. in diameter covered only by peritoneum (Fig. 2). The under surface of the extremity of the tube is roughened where it has been attached to the peritoneum of the pelvic floor. The tube was not opened until hardened. Sections near the uterus show that the lumen is fully 1 cm. in diameter

and that it is filled with a friable, porous, granular looking growth which is free on the under side, but intimately blends with the upper or convex side of the tube. Sections near the outer end of the tube show that the walls are not over 1 mm. in thickness. Here also the tube lumen is filled with a similar friable growth which is whitish yellow or mottled, evidently as a result of old hemorrhages. The tube itself is nearly as large as the uterus.

The left tube is about 5 cm. in length, is slightly beaded, and varies from 3 to 5 mm. in diameter. The fimbriated end is patent and the tube has grown fast to the lower and outer end of the right tube. The right ovary is very small, is approximately 1.5 by 1 by 1 cm. The left ovary is also atrophic, being

of the portion removed, in its fresh state, was about six inches. The rectal mucosa is smooth and apparently normal. The constriction was due to infiltration of the adipose tissue surrounding the rectum. The nodules in the omentum, as noted in the clinical description, are firm. Some of them reach fully 3 cm. in length.

Histological examination.—Sections from the uterus show that the surface epithelium is intact. The glands are normal. At numerous points the muscle is becoming active and growing up into the stroma. It shows us fairly well how an adenomyoma may develop from an in-growth of the muscle fibers.

Sections from the tube near the uterus show that springing from the upper wall of the tube is a new growth, as indicated

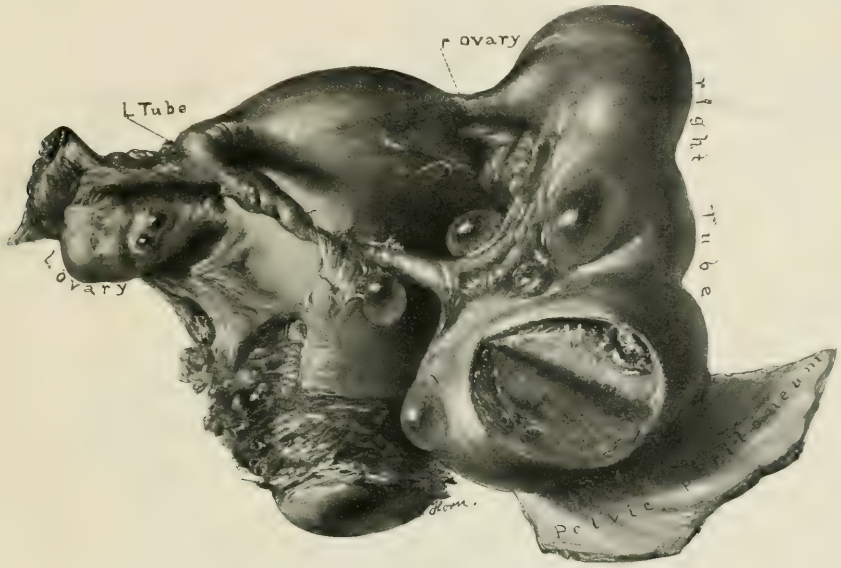


Fig. 2.—Primary Carcinoma of the Right Fallopian Tube. (Natural Size.)

The right tube at the uterus is normal in size. It soon, however, suddenly becomes much enlarged, is somewhat lobulated, and finally terminates in an occluded fimbriated end 4 cm. in diameter. For the most part it is smooth, but at several points are cyst-like elevations. Here all the muscular coats of the tube have given way, and there is bulging of the tubal peritoneum. The tubal growth is solid and granular as seen where the tube is incised. Attached to the lower surface of the tube is a large flap of pelvic peritoneum.

The left tube is small, passes backward and joins with the occluded and enlarged right tube.

Both ovaries are very small, but on histological examination they were found riddled with cancer. It was impossible to satisfactorily remove the extensive carcinomatous growth of the tube and six inches of the bowel without also doing a complete hysterectomy.

2 by 1.5 by .6 cm. Attached to the right side of the cervix is an irregular area of peritoneum which was approximately 7 by 6 cm. The central portion of this is hard and indurated, the outlying portions are smooth.

The rectum is atrophied to a considerable extent. The length

in the gross description. The lower part of the tube is free. Projecting from the side of the tube where the lumen is free are little finger-like outgrowths lined by a single layer of delicate epithelium. The nuclei are oval and vesicular. Some of the nuclei stain very deeply and are rather increased in size.

They immediately remind one of a malignant growth. Springing from the wall of the tube and filling almost the entire cavity is a papillary growth. The stroma of the out-growth consists of spindle-shaped connective tissue. The epithelial covering is one or many layers in thickness. In numerous places the epithelial covering has greatly proliferated, so we have solid masses of cells many layers thick. Here also there



Fig. 3.—Torsion of an Accessory Omentum.

This accessory omentum was attached near the junction of the ascending and transverse colon and was absolutely independent of the normal omentum. The lower border gives its relative breadth. It has become twisted on itself from right to left several times. At the points of twisting the tissue was bluish black. The pedicle is very small. We have unfolded the lower border in order that the omental structure may be more clearly seen.

On histological examination the tissues presented the typical picture of omentum; the vessels were, however, thrombosed and there was considerable extravasation of blood into the fat.

are large and deeply staining nuclei. In the deeper portion of the growth the connective tissue predominates and we have solid nests of cells. The epithelium tends to retract from the connective tissue. At numerous points large areas of the growth have undergone coagulation necrosis and we have fragmentation of the nuclei. The outer muscular wall in most places is still preserved. At some points, however, the entire thickness of the tube has been involved by the growth. Sections from the outer portion of the tube yield practically the same picture. The papillary arrangement is particularly well marked and many of the nuclei are spindle-shaped or irregular, very large and deeply staining. In some sections fully three-fourths of the field have undergone coagulation necrosis. In such areas only a few of the cells around the larger blood vessels still retain their vitality. Scattered

throughout the muscular walls of the tube are definite masses of growth chiefly in the form of cell nests or penetrating glands and on the outer surface of the tube are little bunches of new growths. We have undoubtedly a primary carcinoma of the Fallopian tube with a penetration of the entire tubal wall at numerous points.

Sections from the right ovary, which was very small, show that the organ in some places is normal, but at many points it has been penetrated by masses of carcinoma which send out branches in all directions. The cells present exactly the same characteristics and are manifest in the depth as well as on the surface. Here also there is some breaking down. The left tube near the uterus is practically normal. The left ovary, although also very small, shows diffuse infiltration by the growth. The structure is recognized as typical, carcinomatous glands or as isolated, large, irregular cells with irregular and deeply staining nuclei; in fact the ovary is riddled by the growth.

Sections from the omentum show a most typical picture. In such areas the fat of the omentum is to a great extent replaced by young and old connective tissue, and lying in the connective tissue are masses of epithelial cells, very solid, with a definite glandular-like arrangement. The same large, deeply staining and irregular nuclei are also here in evidence. The nuclear figures are particularly well formed. Rarely do we find a mass of cancer cells in the omentum without a well-defined area of commencing connective tissue development as in this omentum. We find considerable hemorrhage and also breaking down of the carcinomatous elements. The only extension to the rectum is by continuity from the outer surface. The rectal mucosa has not been involved.

Diagnosis.—Primary carcinoma of the right Fallopian tube with extension to the peritoneum of the pelvic floor, to both ovaries, and also to the rectum by continuity, general pelvic adhesions; extensive metastases into the omentum.

For a further discussion of the various forms of cancer of the tube, we would refer the reader to Dr. Elizabeth Hurdon's article, published in the Johns Hopkins Hospital Bulletin, Vol. XII, p. 315, 1901, and to the recent article by G. J. Tomson, published in La Gynécologie in February, 1905.

III. Torsion of an accessory omentum (Fig. 3) *producing symptom simulating appendicitis. Recovery.*

Mr. E. S. was seen in consultation with Dr. Wm. Wright on March 12, 1905. He is a railroad conductor, 47 years of age, and weighs 180 pounds, has a florid complexion, and is very stout for his height. About six days ago, while upon his train, he found it necessary to put off a drunken man, who suddenly turned and whirled the conductor around twice. Next day he felt a little discomfort in the region of the stomach; on the following day pain over the appendix. When I saw him all abdominal rigidity had disappeared. There was, however, a temperature of 101.5 degrees and his pulse was 100. On examination of the blood it was found that there was a marked diminution in the eosinophiles and a leucocytosis of 17,600. On examining the patient under anæsthesia I failed to find any thickening over the region of the appendix. Nevertheless, I made a gridiron incision, deeming an exploratory section necessary. The appendix was found somewhat thickened and slightly adherent; it was removed. On further examination I found a large area of induration on the right side extending half way between the anterior superior spine and the ribs. The incision was accordingly continued upward as far as the free margin of the ribs. The omentum was found adherent. In order to wall off the parts thoroughly I severed the omentum near the thickening and walled off with gauze. The adherent portion of the omentum was now loosened and removed without any difficulty and with no hemorrhage. On carefully manipulating the area of induration, which was at about the junction of the ascending and transverse colon, I was able to loosen up a very strange looking mass which had a mottled appearance, was grayish yellow, and had fine reddish markings all through it (Fig. 3). One of the doctors present suggested hemorrhagic pancreatitis. On following this mass down to the pedicle, which was about 1 cm. in breadth, it was found to contain two small blood vessels. The mass was tied off and removed. It was situated just to the outer side of the jejunum and was slightly adherent to the gall bladder and had become twisted upon itself and was becoming gangrenous. When unfolded it was found to consist of tissue in no way differing from omentum. Where it had been folded upon itself the parts looked gangrenous. These areas were bluish black in color. The gall bladder was normal.

The patient made a very satisfactory recovery. When last seen, in October, he was in excellent condition.

Gyn.-Path. No. 8114. The entire specimen is fan-shaped when partially unfolded. It is 14 cm. in length, and at the lower margin reaches 12 cm. in breadth. The edge is sharp. On section the hardened specimen is brownish-black, evidently due to thrombosis of the blood vessels.

On histological examination the growth proves to be omentum. The blood vessels are much distended and the blood is apparently coagulated. There is considerable hemorrhage into the adipose tissue surrounding the vessels.

In this case the symptoms were very suggestive of appendicitis, and without an exploratory operation the true condition of affairs could not have been ascertained. With the abdomen open this hard growth felt very much like a nodular, carcinomatous mass, and even when the incision had been lengthened inspection of the growth strongly suggested malignancy or acute pancreatitis. An accessory omentum is, to say the least, a very rare condition. Had this accessory omentum remained in much longer, total gangrene would undoubtedly have occurred.

A CASE OF SARCOMA OF THE EYE, INVOLVING CHIEFLY THE CILIARY BODY.[1]

By Paul G. Woolley, M. D.,

Director Serum Laboratory, Manila, P. I.

(From the Government Biological and Serum Laboratories.)

For the history of the following case, and for the small growths removed from the site of a previous operation, I am indebted to Captain Stiles, Assistant Surgeon, U. S. Army.

The pathologic specimen was sent to the Biological Laboratory in Manila from the Civil Hospital.

The case was that of one T. F. H. D., an officer in the Philippines Constabulary, who on the 13th of January, 1903, was struck in the eye by a bamboo stem. A thorn of the stem penetrated the right lower lid near the outer canthus, without, so far as can be determined, injuring the globe. Some inflammation of the lid and conjunctiva followed the injury, but this was transient and the part remained apparently well until March 10, 1903, about two months after the injury. At that time, following hard work in the field, the patient experienced some photophobia, but he noticed no impairment of vision. Toward the end of April, *i. e.*, in the fourth month after the injury, he began to have slight pain in the globe, with severe headaches, and vision was so impaired that the eye could not be used for aiming firearms. From that time on vision steadily became worse. By the middle of July there remained only light perception, and the pain in the globe was so severe that sleep was interfered with. The patient was then transferred to Cebu for treatment. Before he reached that point, however, vision had improved to a slight extent, but the pain was undiminished.

On August 19, 1903, about seven months after the injury, the man was admitted to the Civil Hospital in Manila. At that time the pain in the globe was constant and severe, he had considerable headache, and of vision there remained but light perception. Ten days later the injured eye was totally blind.

On September 23, 1903, somewhat more than eight months after the injury, the right eye was enucleated. Convalescence occurred with no complications.

Six weeks after operation a small mass of granulation tissue appeared in the line of the cicatrix in the conjunctiva. This increased slowly, and on one occasion bled spontaneously but only enough to stain the conjunctival secretions. About six weeks later (December 22) another small mass appeared to the outer side of the first growth.

When he was seen by Dr. Stiles on January 4, 1904, there were two rounded masses of soft tissue, each about 3 mm. in diameter, growing from a common pedicle which measured less than 1 mm. in width, and springing from the cicatrix resulting from the "pucker string" suture of the conjunctiva made at the time of enucleation.

These growths were of the color of the rest of the conjunctiva, were not macroscopically vascular, and not at all painful. The growth of the outer and more recent of the two masses had been much more rapid than that of the original one, and the two growths were of about equal size when seen. The patient said that he had had some pain in the head, back of the eye, but none in the orbit itself.

The lower palpebral conjunctiva was slightly follicular, and there was free purulent secretion from the orbit.

These growths were removed, the pedicle touched with pure carbolic acid, and the orbit irrigated for two days. The growth proved, upon microscopic examination, to be composed of granulation tissue infiltrated with leucocytes, and with no evidence of any other neoplastic process.

The right eye, sent to the Biological Laboratory, had been opened and showed a thickening, extending over three-fourths of the circumference of the eye and localized distinctly (macroscopically) to the region of the ciliary body and the immediately adjacent portions of the chorioid. The growth was thickest just posterior to the corneo-scleral junction and just at the insertion of the iris, *i. e.*, in the region of the ciliary body. It was whitish in color and had no macroscopic evidence of pigmentation. In one place there was some staining as from hemorrhage.

Pieces of the tissues were fixed in Zenker's solution, imbedded in celloidin, and stained with hæmatoxylin and eosin, safranin, methylene blue, thionin, and Mallory's stain for reticulum.

The cornea and retina showed no variation from normal. The blood-vessels of the conjunctiva were distended and there were small hemorrhages into the substance of that layer, and into the subconjunctival tissues. About the deeper vessels there was a well-marked infiltration with round cells, which in their arrangement in more or less definite rows and from their position about these blood-vessels seemed to have some relation to the perivascular lymph spaces. The nuclei of these cells were for the most part deeply stained, but the protoplasm was relatively abundant. Other cells showed all the characters of the lymphoid cells of small round-celled sarcomas. These lines of cells were separated by a well-developed fibrous tissue.

The sclera was normal except in the region of the corneo-scleral junction where there were occasional lines of the cells described above, and these were also present about the blood-vessels and along the lymph spaces. This infiltration with

[1] Read at second annual meeting of the Philippine Islands Medical Association, March, 1905.

round cells was especially well marked in the region about the canals of Schlemm.

The chorioid was involved in the small-celled infiltration and the whole width of this coat was involved for at least a centimeter posterior to the ciliary process. The infiltration farthest from the ciliary body was confined to the inner layer of the chorioid. In these inner parts of the chorioid layer the growth showed a considerable number of pigmented cells, of spindle or angular form and evidently of connective tissue origin.

In that part immediately in the neighborhood of the ciliary body the growth had an appearance unlike that seen in other parts of the tumor. There, at first sight, the picture was that of a small, round-celled sarcoma, but another type of cells was also present, cells that were separated by healthy looking connective tissue into alveoli and columns. Many of these cells were typically epithelioid in appearance and strongly resembled those of perithelial sarcomas. The growth was certainly not endothelioid in the narrow sense of the word, and in no place was there any evidence of vascular endothelial proliferation. The individual cells were polyhedral, with abundant protoplasm that stained well with acid dyes, and had round vesicular nuclei. They are probably of perithelial origin. There was no increase in the muscular elements, no evidence of myomatous growth, and in cross and longitudinal sections the Mullerian fibers appeared normal.

It was in the sections stained by Mallory's method that most light was shed upon the nature of the tumor. In such preparations it was seen that there was a well-marked and complete intercellular reticulum. This reticulum was so arranged that certain of the cells were arranged in complete columns, between the individual cells of which there was a very delicate meshwork. The reticulum between the columns was coarser. But in other places there was a complete lack of orderly arrangement, and in such areas the cells were closely packed together, but each one was surrounded by a very delicate reticulum.

I incline to the opinion that in this tumor two types of tissue participated, one a pure undifferentiated connective tissue, the other perithelium, *i. e.,* those cells forming the lymph spaces about the blood-vessels.

In the literature on tumors of the eye, to which I have access, there are comparatively few cases of leucosarcomas originating in the ciliary body. Parsons (Arch. Ophthal., 1903, LV, 350) gives a short resumé of certain of these cases, but with especial reference to the so-called "ring-sarcomas" of which, in a way, the present case is an incomplete example. In all probability if the growth in this case had been allowed to proceed for some little time longer the whole circle of the ciliary body would have been involved. Parsons' case was one of spindle-celled sarcoma in a youth 14 years old, and was circumstantially inaugurated by a blow upon the eye.

In Jano's case, so far as Parsons' abstract is concerned, at least, no cause is given to account for the growth, which occurred in a 10-year-old girl and which was composed of spindle cells, and with, apparently, no involvement of the chorioid.

Hoensell and Fienzel reported a case of sarcoma in a woman aged 43.

Groenouw's case occurred in a man 28 years old, following a blow upon the eye. The tumor was first noticed three weeks after the trauma. In this case the cells composing the growth were of endothelial origin.

The case reported by Kerschbaumer occurred in a man of 27 years, and was composed of large round and oval cells.

Myerhof observed an unpigmented tumor in a man 72 years old, and also a circumscribed alveolar endothelial sarcoma of the ciliary body in a man of 50 years.

These cases with his own are the ones which Parsons thinks the only ones of undoubted leuco-sarcomas of the ciliary body. To this list may be added, I think, the case reported here, for here as in Parsons' case the true tumor cells are unpigmented, and the cells that show granules of pigment are in direct relation to the pigmented portions of the eye. Moreover, they have none of the character of the tumor cells. But there is a certain unique feature in this tumor in its composition of cells of connective tissue origin and others of apparently perithelial derivation.

As for the etiology of sarcomas of the uveal tract, there is some difference of opinion. In the present case, at least, the growth may be referred to the injury caused by the bamboo thorn. But in the statistics of Treacher Collins, trauma could be established in but seven cases of 103, or 6.79 per cent.

Seven months after the enucleation I met the patient at his post in one of the provinces. He was perfectly well, with no sign of recurrence and no symptoms of any disturbance about the wound or orbit.

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RENAL DECAPSULATION IN NEPHRITIS, WITH REPORT OF A CASE.[1]

By Henry Harris, M. D.,

Instructor in Principles and Practice of Medicine, Cooper Medical College, San Francisco.

Upon the clinician falls the work of deciding whether renal decapsulation in Bright's disease is of value. For this form of treatment has certainly gained sufficient favor to be always considered in any case of this disorder. Upon the clinician will also fall the decision concerning the advisability of operation, because to him the patient first comes. The subsequent results in every case are of value to the profession, especially from the clinical side. For the operation being over, our judgment of the result is based on data obtained through methods of clinical diagnosis. A careful diagnosis of cases operated on has not always been made; this is particularly apparent in the early cases reported.

Any discussion concerning the pathology of renal decapsulation seems at present premature and unnecessary. Whether by lowering renal tension, by establishing collateral circulation, or through beneficial nervous influence the desired result occurs, is undecided. More autopsies on such subjects, particularly on those dying by accident or by intercurrent disease, will ultimately help to decide this question, if it does not entirely decide it. Animal experiments done with the view of studying the effects of decapsulation have shown that a new capsule is formed in dogs and rabbits in about three weeks. On fifteen dogs Dr. H. Johnson (1) showed at autopsy that sufficient anastomosis had not occurred between renal and perirenal blood vessels to influence the renal circulation. His results are well known in this country. Quite opposed to his findings are those of H. Stursberg (2) (Bonn), and of B. Asakura (3) (Berne), results which are not so well known in this country.

Stursberg, attempting to imitate the nephritic conditions found in man, treated dogs and rabbits with doses of potassium chromate. He does not believe, however, that the chromate exerted any actual influence on the result of his experiments. In from four to nineteen weeks after decapsulation the animals were killed by bleeding from the carotids, were then hung up with the head downward, further ridding the body of blood, and then they were injected through the aorta with a gelatine mixture. Especially in those cases where nephropexy had been done, it was possible to make out a considerable increase of capillaries and even an increase of larger vessels. This might be seen macroscopically, but was easier to discern microscopically. Not alone could the injecting fluid be pushed from the kidney outward, but even with the renal vein and artery cut off the fluid penetrated from without inward along small branches as far even as the medullary substance. On a normal animal the last procedure also showed a penetration of the injecting fluid, but not in the same degree. He therefore believes that by decapsulation sufficient new formation of blood vessels occurs between kidney and its surrounding parts to actually influence the flow of renal blood, at least in animals. If the renal circulation be faulty, the result might be more marked. He thinks, too, the operation in man acts beneficially because of the new formation of blood vessels, though in acute cases relief of tension is also a factor.

Asakura also found a considerable anastomosis to have occurred after renal decapsulation on rabbits and dogs. His work was, however, rather directed towards showing that the procedure was without particular danger to the kidney. Seven days after the operation slight evidences of renal trauma were found, consisting of small hemorrhagic areas with pus cells. He tested also the resistance to bacterial infection of rabbits whose kidneys had been decapsulated. Such animals actually lived longer than control animals not operated on. Even if the kidney were already infected by pyogenic organisms and decapsulation was then performed one, two, or three days after inoculation of the rabbit, the animals lived just as long as control animals whose kidneys had not been decapsulated. Still after all has been said from the experimental side the question as to the ultimate value of the operation must rest on clinical experience.

Clinical experience with this procedure has now grown to very respectable proportions, the literature being quite vast. The names of Edebohls, Ferguson, and Reginald Harrison must be referred to in this connection as pioneers. An extensive bibliography is here superfluous; for this the reader is referred to a paper by G. F. Suker (4). The value of treatment of decapsulation is disputed by many; Rovsing (5) (Copenhagen), for instance, claims that the apparent benefit following operation is due entirely to the rest in bed. This is in contrast to the optimism shown by others, Edebohls (6), Guiteras (7), Tyson (8). A study of the literature will show, however, a growing belief in the efficacy of the operation in selected cases, particularly in those cases in which the cardiovascular system is not yet especially injured. The value of the procedure in extreme cases, as of urinary suppression or of severe uremia in the course of chronic nephritis, is generally conceded. Lennender (9) (Upsala), Whitacre (10), Goodfellow and Eaton (11). The last two observers operated with spinal cocainization. Writers are not agreed as to the form of chronic nephritis most favorable to this procedure, and this question is made still harder to decide by the lack of uniformity among different pathologists and clinicians in designating the lesions encountered.

The following case is presented because the writer believes it has proven one particularly suitable to observations over a

[1] Case demonstrated before the San Francisco County Medical Society, May, 1904, and before the Cooper Science Club, May, 1905.

long period. Altogether the case has been studied twenty-three months, sixteen and one-half months after bilateral decapsulation had been performed. In the examination of urine only those methods were followed easily available to the practitioner. Albumin was determined by the Esbach tube, urea by the Doremus apparatus. While in the hospital a mixed sample of the twenty-four-hours output was used for analysis; after the patient left the hospital, the afternoon specimen freshly passed in the office was examined. The patient was given a graduated cylinder with which to measure the total twenty-four-hours output at his home. At stool, the patient used a separate urinal, so that no urine escaped unmeasured. Microscopic examinations were made only of centrifugalized specimens.

The patient, an intelligent Chinese-American, twenty years old, first presented himself for treatment at Lane Hospital, San Francisco, June 6, 1903. In his history there was nothing indicating the cause of his illness. Six weeks before, his face swelled, then his abdomen, feet, and legs. He had become constipated and the amount of urine had decreased.

Physical examination on the following day showed patient in bed, comfortable, no dyspnœa, face and eyes puffy, fair color, tongue heavily coated. Pulse 84, regular in force and rhythm, fair tension and volume. Artery wall felt. *Chest:* expansion fair, vocal fremitus absent in lower part of chest, on percussion skodaic resonance above fourth rib, below this the note is dull at the fourth rib in an erect position and at the sixth rib when he is reclining. Dulness reaches the fifth dorsal spine posteriorly. Breath sounds roughened above this line of dulness, distant and weak below it. *Heart:* point of maximum impulse within the mammary line, relative cardiac dulness begins at fourth rib, extends seven centimeters to the left and three centimeters to the right of the median line. Sounds clear, of normal relative intensity.

Abdomen much distended, movable dulness in midline, four centimeters below the navel.

Lymph glands not enlarged. Legs, scrotum, and penis very markedly edematous. Edematous cutaneous striæ marked on the right side of the thigh.

Urine.—Amount of 24 hours' urine, 420 cc., albumin 3 per cent. He was tapped and given dietetic (light diet) and medicinal treatment. Daily sweat baths preceded by pilocarpin grain ⅛ with enemata of iced water one pint every three hours were ordered. After one month his condition was practically unaltered. On June 25, urine output was 360 cc. Six weeks after admission he slowly began to improve. The largest daily output of urine was 1800 cc.

He remained in the ward two and one-half months, during which period he was tapped five times, 3600 cc. of slightly turbid fluid rich in albumin being obtained at one tapping. The left chest was aspirated once and one liter of serous fluid was removed. On leaving the ward, August 21, 1903, the patient felt strong, his face was peaked, he walked about with no consequent swelling of the ankles, his ascites was slight if any, his chest clear. Pulse 84, regular in force and rhythm, low tension. Diagnosis of case, chronic parenchymatous nephritis.

Although resting and taking dietic and medical treatment at home, he steadily grew worse, as did also the urinary conditions. In six weeks it was again necessary to send him to the hospital. He entered on October 5, 1903, in somewhat better condition than at his first admission, but he was still in a serious state. His second stay in the ward lasted two weeks. Upon his discharge he was slightly improved, although his ascites and anasarca were still evident and the urinary condition was practically unaltered. One month after this, November 19, 1903, he entered the hospital for the third time in four months with marked anasarca, ascites, and hydrothorax. His urinary condition was very bad.

December 16, 1903, patient's anasarca and ascites were about the same as at admission on November 19, 1903. Daily output of urine varies from 130 cc. to 920 cc. Condition of patient was serious, for he had not responded to dietetic or medical treatment, hot air baths, and the usual diuretics and cathartics. Surgical procedures were now deemed worthy of trial. He was transferred to the surgeons with the following summary concerning the case:

"Diagnosis of case, chronic parenchymatous nephritis, with ascites, hydrothorax, and anasarca. The cardiovascular apparatus is not appreciably affected."

Urine of this date, Dec. 16, 1903, showed the following conditions: Total quantity, 330 cc., acid, dark, cloudy; albumin, 1.4 per cent; urea, 8.8 gm. Large number of hyaline, granular, epithelium, leucocyte, and fatty casts. Epithelial cells detritus and mucous cylinders.

Patient was operated on by Dr. S. Stillman on December 17, 1903, under ether anæsthesia. Time of operation, one hour. The abdomen was tapped and both kidneys were decapsulated. The kidneys were of medium size and pale, the capsules were wrinkled and not adherent. Patient stood the operation well. On returning to the ward his pulse rate was 96, weak, but regular. The first day after the operation the patient was catheterized and also voided urine, total amount being 298 cc.

On the third day the total output of urine was 100 cc.

The patient continued in practically the same condition as before the operation, in spite of fluid diet with flaxseed tea and buttermilk. On December 30, thirteen days after the operation, because of abdominal discomfort, he was again tapped and 3650 cc. fluid were removed.

Upon January 7, 1904, diuretics, caffein, spartein, and strychnine sulphate were resumed with no increase in the output of urine.

January 10, the output of urine was 450 cc. and the patient's condition was distinctly unsatisfactory, anasarca and ascites being marked. Pulse 92, weak but regular. (No signs of cardiac embarrassment.) Patient complained of discomfort in abdomen; again tapped and 3830 cc. of fluid were removed.

On January 12, condition about the same, swelling of the eyelids marked, visual orifice distinctly impinged on, daily enemata of a quart of iced water were ordered, which probably helped the patient. On the first day of their application the output of urine increased from 390 cc. to 1080 cc., and upon the second day 1040 cc. He was again tapped on January 16, and 4000 cc. of fluid were removed.

After January 12, the output of urine in general increased, and after the last tapping (January 16) he improved gradually.

Upon January 29, 2050 cc. of urine were voided. On this date the enemata were discontinued and the urine continued to be voided in large amounts.

On February 1 he was able to walk about the ward. Pulse 68, weak but regular, low tension. The chest, especially on left side, still contained small amounts of fluid; ascites was still present in slight degree; dulness reaching three centimeters above pubes; slight edema of legs and genitalia.

February 10; there has been steady improvement, no ascites, no hydrothorax, no edema of face or thighs. There remains a slight pitting on pressure about the ankles. No subjective symptoms. Output of urine good.

Patient discharged on March 3. General condition good. Face not swollen, eyes normal in appearance. Tongue of good color, clean. Pulse 24¼, regular in force and rhythm, low tension, artery wall just felt.

Chest.—Lungs and pleuræ clear. Heart: point of maximum impulse well felt in fifth interspace within the mammary line.

Relative cardiac dulness extends eight centimeters to left and three and one-half to the right of the mid-sternal line. Sounds regular and clear, normal relative intensity. Abdomen negative, ankles pit very slightly on firm pressure, genitalia not swollen. Blood: hæmoglobin 90 per cent, red blood corpuscles 4,500,000. Patient is to continue light diet at home and is given directions as to the use of enemata for moving bowels.

April 1. Patient feels well and is now working in a newspaper office as translator. Physical examination shows considerable pitting at the ankles, which has increased gradually during preceding month.

There is no ascites or puffiness of the eyes.

May 9. Feels well, working several hours a day. Slight pitting at ankles. Otherwise negative.

May 21. Looks very well, works four to five hours a day, as representative of a commission house. Feels well. Ankles pit slightly. Lower abdomen somewhat dull, this dulness not movable, no distension of abdomen at all.

July 19. No discomfort except slight shortness of breath at climbing up stairs. Bowels move with enemata every other day. Pulse 96, good quality. Heart negative. Abdomen clear, no ascites, slight edema of ankles.

December 10. Physical signs identical to those of last examination, except that there is no edema of the ankles. No edema anywhere. Cardiovascular system normal. Blood: red blood corpuscles 4,600,000, white blood corpuscles 6800, hæmoglobin 90 per cent. Has been doing literary work during the past six months.

February 26, 1905. Patient has been seen several times during the past month; he feels well and examination is negative, except for operation scars and atrophic lines in the skin, resulting from previous edema; urinary conditions have improved.

April 26. Physical examination same as on February 26.

Concerning the Urinary Findings.

At the first admission, June 6, 1903, to August 21, 1903, the daily quantity varied from 360 cc. to 1800 cc.; the amount of albumin from 2.1 per cent to 0.35 per cent. A large number of hyaline, granular, epithelial and fatty casts, much detritus, and many epithelial cells were always present; towards the end of the period casts were fewer in number (especially the fatty ones) and the detritus was less in amount.

In the second admission, October 6 to 21, the daily quantity varied from 200 to 940 cc; albumin content 4. to 0.7 per cent. Microscopic findings identical with those of first admission.

On the third admission, November 19, 1903, the daily amount voided during the first two weeks averaged 920 cc. on soft and liquid diet, with one or two stools daily.

December 3 to December 10, daily average 660 cc.

December 10 to December 17, daily average 418 cc. with albumin 1.4 per cent and total area 7 grams. Microscopic findings as those of first admission.

On December 17, patient was operated on; in the nineteen hours following operation 235 cc. urine was secreted (voided and catheterized); dark, smoky, cloudy, specific gravity 1032, acid, albumin 1.7 per cent, urea 5.8 grams. Microscopically, hyaline, granular, epithelial and fatty casts in immense number; many red blood corpuscles and pus cells, soda urate crystals.

December 19 to 26, daily average 540 cc., specific gravity 1024, albumin still 1.4 per cent, urea 13 grams. Microscopic, hyaline, granular, and epithelial casts present in lessened number; considerable detritus.

December 26 to January 2, 1904, daily average 600 cc., character practically unchanged.

January 6 to 13, daily average 533 cc., character practically unchanged.

On January 8, fatty casts were seen for the last time.

January 13 to 20, daily average 973 cc. Albumin 0.5 to 0.8 per cent; urea 8 to 12 grams; fewer casts, and these mainly hyaline and granular. Iced enemata started on January 13.

January 25 to February 1, daily average 1774 cc. On January 28, specific gravity was 1010, albumin 0.5 per cent, urea 9.6 grams. No casts were found (no doubt due to alkaline reaction).

January 29, iced enemata discontinued.

February 1 to 8, daily average 1820 cc.

Examination of February 5: Amber, clear, neutral, specific gravity 1015, albumin 0.35 per cent, urea 9 grams; microscopic, few hyaline and finely granular casts and detritus.

February 24 to March 3, daily average 1945 cc. Examination of March 3: Amber, clear, acid, specific gravity ?, albumin 0.35 per cent, urea 23 grams; microscopic, few hyaline casts, some with fine granules adhering, mucus threads, a few flat epithelial cells and leucocytes, very little detritus.

On March 3, patient left hospital and has not returned. The following examinations were made on fresh specimens passed in the office. The quantitative estimations of albumin and urea are thus less trustworthy.

March 18 to April 1, daily average 1730 cc. Examination of March 19: Clear, amber, acid, specific gravity 1010, albumin 0.12 per cent, urea 17 grams; microscopic, few long hyaline casts, few granular casts, mucus cylinders and cylindroids, few flat epithelial cells.

April 24 to 31, daily average 1390 cc.

Examination of April 28 showed character practically unchanged.

May 8 to 15, daily average 1230 cc. Examination of May 9: Clear, light straw, acid, specific gravity 1015, albumin 0.15 per cent, urea 23 grams. Few hyaline casts, flat epithelial cells, and slight amount detritus.

June 1 to 8, daily average 1350 cc. Examination of June 15: Acid in reaction, uric acid crystals present, but no casts found. Otherwise practically identical with May 9.

Examination of September 17: Clear, amber, alkaline, specific gravity 1015, albumin 0.1 per cent, urea 13½ grams to liter; microscopic, few epithelial cells and leucocytes, but no casts.

December 10 to 17, daily average 1252 cc. Examination of December 10: Clear, light straw, neutral, specific gravity 1005; albumin too little to read on an Esbach tube, urea 15 grams to the liter. Microscopic, few epithelial cells and leucocytes, but no casts.

Examination of December 19: Clear, amber, specific gravity 1021, acid, albumin 0.05 per cent, urea 30 grams to liter; microscopic, few hyaline casts, mucus cylinders and flat epithelial cells.

February 17, 1905: Amber, clear, acid, specific gravity 1014, albumin not readable on an Esbach tube, urea 8.5 grams to liter. Very few hyaline casts and epithelial cells.

April 16 to 25, daily average 1135 cc. Examination of urine April 26: Clear, acid, specific gravity 1020. Centrifugalized specimen showed only a few epithelial cells, no casts. Albumin, trace present, not sufficient to read by the Esbach tube. Urea 16 grams to liter.

Conclusions.

A patient with grave chronic parenchymatous nephritis after being treated energetically by medical measures in the hospital for two and one-half months, was discharged much improved. This improvement was only of short duration. One and one-half months after being discharged patient's condition was again serious and it was necessary to re-admit him to the medical ward.

His second stay lasted only two weeks; at the end of that time his condition was very slightly improved. One month

after this he entered the hospital for the third time, in a serious condition. At the end of a month he had not improved. Bilateral renal decapsulation was then performed. Improvement was noted about three weeks after the operation. In contrast to that of previous admissions, the improvement following operation has been permanent, now lasting sixteen and one-half months and has been very positive.

This improvement is seen both in the patient himself and in his urine. The daily output of urine has increased, the urea has increased. Albumin is present only in traces, and casts are only exceptionally found. Renal decapsulation has been of value in the treatment of this case.

Since writing these notes it is learned that the patient has sailed for Canton, China, in order to take the governmental examinations for a scholarship in this country.

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DR. CHARLES FREDERICK WIESENTHAL'S MEDICAL REPORTS.[1]

BY EUGENE F. CORDELL, M. D.

The following reports of medical and surgical cases were found among the Wiesenthal papers belonging to the late Miss Wiesenthal, of Boston, and by her desire sent to her relations here after her death. They form only a part of the reports sent by Dr. Wiesenthal to his son Andrew, then a student of medicine in London. They are frequently referred to in the letters of the former. For instance, on the 5th of June, 1787, he writes: "I will send you of such Curiosities which occurrd in my practice if you could write something that your Name might be honourably mention by the Revewers. Sometimes a small triffle of that Kind has a great Effect." Again, on the 9th of October, 1787: "In one of the packets I sent you those cases which are somewhat remarkable but in one of them I mean that of Mr. Kervan I will only mention that the quantity of Matter issuing from that Tumor no bigger than a Wallnut was nearly 3 pints. Mr. Kervan was here about 2 hours ago." Again, five days later: "I have sent you various Cases in Physic & will consider of some more, and I think I will likewise send you some of my theoretical Opinions which you may be probably able to elaborate something farther and should it be worth the Notice of some of your friends it might be perhaps worth while to have it publishd for this is Truth that a great many more silly things have been publishd then what we should." And finally in an undated letter, probably about Dec. 1 of the same year: "It would be extremely well to have Something of yours appear in the Magazine. Medical Essay or Observations under your Name as nothing would elate you more. I have sent you several of my Occurrencies & will Send you Some more if perhaps something might be found amongst 'em worthy of attention & which might be plac'd in good Language a piece well wrote & approvd of by the critical Reviewer gives such a Name and Serves as Such an Introduction to a young Man as nothing can opstruct to him."

The originals are copied accurately, the quaint and odd style and spelling giving them, as I think, an additional flavor and interest. They show that their author was an accomplished, judicious, and conscientious physican, and a surgeon of the highest abilities. Unfortunately they were written upon very thin paper which is much worn in the foldings, so that words and indeed whole lines are here and there illegible. We may recall the fact that Dr. Wiesenthal was 29 years old when he came to Baltimore from Prussia. These reports form a good appendix to the "Sketch" of this worthy old physician, "The Father of the Medical Profession of Baltimore," published in the BULLETIN of July-August, 1900.

[CASE I.] *An Extravasation of Blood to a great extent under the dura mater without interrupting the animal nor Vital functions by its pressure on the brain.*

A Servt. Woman of Jacob Mayers much addicted to Liquor was for some days supposd to be in Liquor, and I myself when I was calld to see her found her Actions correspond therewith, that forcd Smile or grin which intoxicated people generally have with incoherent Speech as if not in her Senses, and otherwise made me think that she had probably a bottle hid, but being watchd and in 3 or 4 days making only her Water involuntary she expird. we had reason to Suppose Something to be the Matter with her head and having receivd Six months before a blow on the head; her Master [consenting for the Calvarium] to be removd, we found all the Vessels big & small of the dura mater stro

[1] Read before the Johns Hopkins Hospital Historical Club, November 9, 1903.

ing with blood. and of a brown or black or dusky. I cut through it and to my Surprise discoverd a very compact hardish body, which by extracting it became distended and moore loose, not unlike a Spunge which from imbibing Moisture encreases in Bulk, and this being grumous blood destitute of all Serum, which no doubt for the Time it had lodgd there was separated therefrom and enterd the Circulation, and as this blood in its extended form was exceeding the bulk of 2 fists doubld and weight nearly seven or I think nine oz. and therewith at least 5 or 6 days the Animal and Vital functions were sustaind a phenomenon allmost incredible and J freely declare that it would by me have been Scrupled if J had heard Such a Case related as to its Veracity but as it is Fact I must submit it to the reader.

[Case II.]

Jim was an Irish Lad about years old a sturdy young fellow of a [good] Size, who had an Intermittent of which he was curd but complaind of a great palpitation of the heart which he had been troubld with for Some time previous to the Intermittent, this Palpitation encreasd to that degree that it was Seen and strongly felt | nay it could often be perceivd by the Ear | a Sort of a Sound | and he was never easy except when he pressd the Side of his breast against a Chair, his pulse was very irregular generally Small pulsations but now and then very strong Strokes, we apprehended an Aneurism in the Aorta, the Symptoms encreasd daily and his Legs became oedematous. we waited daily for the Catastrophe of the Aneurisms bursting but he died without it, the people being willing to inspect it. I opend him and found the Viscera all in good Order (*except the the ac glands much enlargd and indurated.*) but when the Thorax was examind the heart was of a most uncommon bulk, and nearly as big as a Small Bullock's heart. The Left Ventricle was amazingly long and to this Maisure

THE LENGTH OF THE VENTRICLE

and the Diameter was

THE DIAMETER OF THE LEFT VE

and a very strong polypose Concretion about three inches within the heart very fibrous and fleshy and so as it proceeded in the Aorta of a grey bluish Colour but very tenacious attachd by very thin fibres so the Ventricle Spreading itself broad.

[Case III.] *The Case of a large piece of the os femoris being taken out entire which having been Detachd both above and below from a new Bone and pushd out.*

You perfectly remember our old Negro Harry when in the year Sixty three he belongd to Mr Saml. Young and having an Obstinate ulcer above the Knee was given me under my Care and for better dressing into our house. J perceivd 2 or 3 small ulcers and found the os femoris carious. J put him under an Alterativ Course, and directed his Diet. the fellow being willing to get well was disposd to subject him self to that Regularity so uncommon in Negros,—After about 3 months proceeding in the Method J discoverd a Splinter to be felt which proceeded gradually to come out to a full Sight and by slow degrees in about 3 months

and appeard to be a large portion of the Bone, and quite immoveable. it was quite in the way but from its immobility I presumd justly that a large portion was behind to the extracting of which J deemd this to become a good handle, still having the Idea of a large Splinter. and to facilitate its being more easily taken out J laid the whole Lenght to about 5 Inches lenghtway open, but although the Opening large and kept so the Bone was yet immoveable. it proceded to appear Sideways not unlike a Boar's Tusk. and though every Day more and more it was tied and firm till after a whole twelve Month it became moveable more and more but could not be extracted by a moderate force, the wound was dilated still more and finding the probe to proceed easily largely up along Side of the Bone so that a pair of strong Forceps put up making a good and firm handle for that part which stuck out we extracted of the whole and solid os femoris near Six inches long, my Surprize was great and J was struck with a Notion that although a Small Callus was formd the Thigh would inevitably break, but notwithstanding my Caution to the fellow, he from his feeling being so strong walk on and continued So. the Wound heald up and I bought him afterwards as a Curiosity but although such Similar things have been recorded, what is to me deserving Notice in this Case is that he kept always walking and working on from first to last without even one Single Days laying by. The Bone was intire with the round pipe for the Marrow, and it is clear that the new Bone issuing from the Sound part gradually pushed the faulty out of its place much like new ones pushing the old ones forwards and this way more and more the whole was filld up, to which no doubt my not urging it too intensely but giving it Time for its formation did greatly contribute to.

[Case IV.] *The Case of the Brachial Artery being totally tore.*

[Also marked on back of sheet—Case of Aneurism.]

I was calld to a frenchman, by a french Surgeon who had for the Space of a Week dressd and treated a wound in the bent of the Arm, from the bursting of a Gun which being shatterd all to pieces had wounded the Arm in 2 places across Seemingly altogether but very Superficial, and though nearly as he thought heald. the Arm below became daily more insensible and cold. on examining J found the parts without any Inflammation, and totally without all pulsation in the Wrist. on the Inside of the Arm below the bend, was a large bag likewise without inflammation and pain manifestly containing by its fluctuation a fluid, and above the Arm about the biceps a hardness. an aneurism was to be apprehended. and I prepar'd the apparatus for the Operation. and thought it expedient first to open the bag below within the Arm. which I did intentionally to have room for farther Examination very large, but what was my Surprize when—immediately fresh Arterial blood gushd out. but not by pulsatory Saltations but as if it was pourd out of a Vessel; the Tourniquet which happend previous to have been applid was immediately Screw'd. and after emptying the back of a great portion of grumous blood in Clods and along with it large pieces of the Artery in torn pieces still So considerable that it could be known and examind to be certainly the artery especially by its transverse coat; by introducing my fingers, I could reach up as far as the biceps where I pulld out a large Splinter of the Gun of the Lenght at least of 4 Jnches, and as the Jnteguments were all Separated from the Muscles J could with my fingers reach on the opposite Side of the Arm Sideway of the triceps, and there pulld out a much longer Splint of wood, and it was Amazing that in that Situation for a whole week past the 2 small wounds through which these 2 Separate Splints had passd nearly heald up. and no Jnflamation appeard all the while, but in Order to proceed in the Operation the Tourniquet was slakend not a drop of blood issued. I now desisted from doing anything respecting the Aneurism but on considering all the Circumstances. the Extent of the Wound within, the Lenght of Time. the coldness of the lower part. of the Arm—the want of pulsation, had reason to Suppose that nothing but an Amputation would Save his Life. and prepard the mind of the Patient accordingly for it. but to convince the poor Man that we were not prone to deprive him unnecessary of his Arm. J engaged my honour that J would deferr the Operation to the farthest Minute to See if anything should discover itself. the Wound being So extensive was well cleansd from everything foreign that was containd in it. and from the pieces of

the Arterial Coat I could judge that the Artery was destroyd at least to the full Extent of 4 or 5 Jnches. it was certain that the grumous blood and Splint for the Time stopt the farther effusion of blood from the Artery but when the large Jncision was made the clotted blood took by its coming away the pressure agt. the Artery off So that the blood freely issued along with the grumous blood, but it is difficult to be accounted for, that afterwards on slackening the Tourniquet or even after not a drop of blood should flow or appear. but should I offer my Sentiments on this Phenomenon J should think that although the impelling force was at first Sufficiently strong to protrude a quantity of blood, but that allready for Some day past Nature had attempted to form a new passage through a branch above the torn Artery as it often happens; and as the remaining Artery had for Some distance lost its contractility the impelling force could not continue to be So forcible as at the first onset, but became moreover inclind for forcing a New passage & thereby lessend the impulse still more. We were very Attentive and in 16 hours after the first dressing. a faint pulsation was observd by one of my young Students who was placd there on the Watch, this happy presage. So enlivend the drooping Spirits of the poor patient. and gave now all the Expectation So triffling Small the pulsation was at first it became more and more conspicuous. and in short the Limb was saved. The Wound now heald without impediment, but remaind smaller for Some time the Insensibility was removed in Some Degree. he was able to go to Sea in quality of a Steward. and recoverd during 6 Months part of the Stiffness of the Limb as well as feeling Since which I never heard of him.

1786 [Case V.]

Monday the 20th of March my Son Andrew complaind of being unwell with a head Ake and a fever the Weather being moist and he exposd to it led us to Suppose that he had taken a Cold. and he had a pediluvium applied in expectation of being better in the Morning. but the fever continuing and rather encreasd and a Nausea he was apprehensive of having contracted the Contagion of a Malignant fever which then was very much prevailing in the poor house and being on Acct of the unfavourable Circumstances of being so crowded and badly provided the more assiduous of aforded them Relief he slept but indifferent being pesterd with disagreeable dreams during the Night.

Tuesday. he was not at all refreshd the headache continued but the fever had remarkably diminishd and although he had a Nausea. he objected to an Emetic but chose in preference to take a purge, which operated well but aforded no other Relief his fever returnd, and slept the next night but uncomfortable the saline Draughts were taken. but in the morning.

Wednesday. his fever seemd to intermit So that he took 3 doses of Bark, the fever intermitting nevertheless did not aford much Relief he was heavy. felt disagreable and especially the head ake remaind very troublesome but in the Afternoon the fever returnd with a strong pulse a Dejection of Spirits. which was ascribd to his Impatience on Seeing the fever return when from the Intermission in the forenoon he had flatterd himself of being nearly well or that his Complaint was only a vernal Intermittent nay So mild were the Symptoms that nothing dangerous was apprehended, the Nausea continued and head ake likewise the heavy dreams so that

Thursday in the morning he took 3ij of the Vin. Antimon but from a childish Reason could not prevail on him self to drink the least warm Liquid in order to dilute the Bile which was thrown up in a large quantity the Throat was vellicated there from. he continued Sick at his stomach and felt himself more uneasy head ake continuing a greater debility and a Slight Delirium, the apprehension of contagion from the poor house Seemd to be revivd The Delirium encreasing and although the Symptoms were otherwise as yet very mild. there was rather Reason to apprehend Since in proportion to their Mildness he ought to be able to walk about and he appearing rather in other Respect worse, that at once they would appear in their real force. his fever was now constant the pulse weak the Surface of the whole Body dry a stupor head ake and allmost perpetual Sleep. but this Night he had an

Friday universal Sweat he had taken in small dose of the Vinum Ane. and as he had yet then Nausea. he took another dose to provoke a Vomiting but in no better Mode nor with better Success. the Symtoms seemed to remain at a stand still.

Saturday when we were again flatterd the perspiration keeping on and we did ascribe it to the Antime. wine the only trouble Some Symptom was a perpetual burning at the Stomach that whatever he receivd burnt him, it was my Opinion that as he never disengagd the Bile from the Stomach the Same being very acrid gave to the Stomach that uneasy burning Sensation. he now took the Saline draughts. but the fever now continued. he became more delirious. and manifest Signs of Malignity appeard. Doct Brown was so kind to visite us on

Sunday and thought the Saline Medicine the most proper but as Soon as possible to pour down as much Bark as possible with Wine. it was however difficult to give him either the Wine especially he detested. The Debility was most amazingly great. Delirium continued. his Anxiety was great, and the appearances in general very unfavorable. the pulse very small and at 120 in a Minute. a perpetual Watchfullness with a Stupor. or very interrupted Slumber it was with difficulty he could be prevaild upon to take any Wine although So strongly indicated. the State of insensibility made his fate very precarious—and continued to

Monday in the Same Manner. with clammy Sweats and Blisters were applied without Reserve.

Tuesday a Subsultus Tendinum was perceptible. the Musk was exhibited. and at Times a little Wine mostly by Deception was got down. Doct. Brown now despaird on his Recovery. we thought that probably a little Opium with Camphor would allay the Subsultus & which actually had a visible effect—and more blisters were applied. on

Wednesday he Seemd a little more refreshd and freer from the Delirium the Watchfullness which hitherto had followd the Drowsiness whic he had in the beginning now wore off and he Slept by intervals. the Subsultus lessend and on

Thursday he fell into a profound Sleep. and a profuse Sweat. he now rejected all Medicine and with great persuasion we could get him to take the Bark. th blisters became Mattery and on the whole we had a glimmering of hopes. the Alvus was kept open by glysters but during the State of Insensibility and delirium the Stools were involuntary.

Friday he still perspird constantly on but the Urine had no Sediment the Sound Keeping Suspended and the Colour of a high Orange yellow.

Saturday he was visited by Doct Troop who likewise wishd to have him drink plenty of Wine which we from Time to Time urgd him to but he now became morose and less tractable still now and then delirious, the Doct pronounce him past recovery, without the Wine. but whether it was to give a Refutation to the Doctors Prognostic he seem the following Night better slept more Serene an on

Sunday was so as to give us certain expectation of Recovery. his pulse becam fuller Softer and fell to 90. he took a little Broth and Sago with Some Appetite and drank of Water impregnated with fixt air. with which he continued to recover gradually to our great Satisfaction. [Dr. Osler is of the opinion that this case was one of typhus fever.]

The above is endorsed on the back "Case of Doctor A. Wiesenthal."

A LETTER TO THE GRADUATES OF THE JOHNS HOPKINS MEDICAL SCHOOL.

CHRIST CHURCH, OXFORD, October 30, 1905.

My dear students:—Last evening I was told that a box had arrived from America, and in a few minutes there was brought in a handsome quarto volume with an inscription on the back—"Collected Papers of the Graduates of the Johns Hopkins Medical School." Naturally, I was delighted, and in a few minutes was deep in the contents of the volume, filled with gratitude that you had so kindly remembered me. When, a few moments later, the man came in and asked if he should bring the others, I looked more carefully at the back and found that I was reading only one of a series of twelve superbly bound quarto volumes, furnished with a good index, and each one with a table of contents.

Many pleasant incidents have happened in the course of more than thirty years' teaching, but I do not remember ever to have been so completely overwhelmed, so to speak, by the character of the gift. Of course I was well aware that, in the few years that had elapsed since its foundation, much good work had been done by the members of the school. No small part, indeed, of your education consisted in helping you to reach the state in which you could become contributors to science, and for this your careful preliminary training, and your course in the medical school had fitted you. But that in so short a period of eight years you should have been able to accomplish so much, is a matter not less of astonishment than of pride. Among the 465 separate contributions an extraordinary range of subjects is considered—anatomy, physiology, pathology, bacteriology, hygiene, general medicine, surgery, pharmacology, clinical chemistry, gynecology, obstetrics, and medical literature. It is encouraging to see that the practical aspects of medicine and surgery have engaged your attention quite as much as the scientific.

The establishment of the Johns Hopkins Medical School was in the nature of a large experiment in medical education. To insure success three conditions had to be fulfilled:—(1) The students had to possess a thorough training in the sciences upon which medicine is based, in addition to a general education befitting men who were to be members of a learned profession. (2) Well-equipped laboratories had to be organized, in which the sciences of anatomy, physiology, pathology, pharmacology, and physiological chemistry would be taught by men who were investigators as well as teachers; and (3) lastly, a hospital to be to the senior students what the laboratories of anatomy, physiology, etc., were to the juniors, a place in which the phenomena of disease, with all their human interests, should be studied under skilled supervision.

These splendid volumes are a striking testimony to the success of an undertaking, which we all feel has already passed the experimental stage.

Two things remain—on your part, to keep up the high standard you have set with the steady energy of men who have faith in the future of scientific medicine and faith in their own powers to help in its progress. By your enthusiasm and unselfish devotion to the best interests of the profession you should stimulate the production of good work elsewhere. What you have done in Baltimore may be done by other students—many of them your own—and by other teachers. The record you have made is unique in the history of medicine in America, but it should not be so for long. In equipment, in methods, and in results, foundations equal to those made by Johns Hopkins are possible in places animated with the spirit of scientific research.

On the part of the trustees and the faculties of the two great institutions, linked together by the Johns Hopkins Medical School, there is the bounden duty to maintain an incessant watchfulness lest complacency beget indifference, or lest local interests should be permitted to narrow the influence of a trust which exists for the good of the whole country.

Though absent in the body, my thoughts are constantly with the school to which I owe so much, and in the progress of which I take so much pride. I hope to be able to return every session for a brief period, and in this way keep in touch with the work of the hospital and of the medical school.

Believe me, my dear students, to be,

Yours faithfully,

WM. OSLER.

VOLUME XII OF THE JOHNS HOPKINS HOSPITAL REPORTS

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V. Typhoid Meningitis. By RUFUS I. COLE, M. D.
VI. The Pathological Anatomy of Meningitis Due to Bacillus Typhosus. By W. G. MACCALLUM, M. D.
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VIII. Renal Tuberculosis. By GEORGE WALKER, M. D.

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PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

October 23, 1905.

Dr. MacCallum in the chair.

Pulsating Empyema. DR. R. I. COLE.

Case 1 was admitted to the surgical wards in April complaining of trouble with his lungs. He had an attack of pneumonia in December, which lasted for five or six weeks and left him weak and failing in strength. Ten days before admission he had marked exacerbations of pain and weakness and continued to grow weaker. His chest was aspirated and a small amount of purulent fluid removed. The entire left side of the chest was bulging, and there was dullness in the left supraclavicular fossa and flatness through the entire left chest below. There was an impulse in the third and fourth interspaces to the right of the sternum. The whole front and axilla of the left chest showed a visible pulsation, forcible, diffuse, and systolic in time. The chest was opened from behind and a large amount of pus removed. The patient left the hospital in good condition.

Case 2 was admitted in January complaining of shortness of breath. He had signs of a pleural effusion on the left side. The chest was aspirated and at different times eleven, twelve, and thirteen hundred cc. of fluid were removed. Tubercle bacilli were demonstrated in the fluid. The patient improved and left the hospital practically well in March. He returned in June with shortness of breath and an irregular fever. A needle was inserted into the left chest and a small amount of bloody fluid was removed, which contained many mononuclear and but few polymorphonuclear cells. About October 1 there was a bulging in the left axilla, and upon October 17 a definite area of pulsation in the third and fourth interspaces outside the mammillary line shown by tracings to be systolic in time. Cardiac dullness reached 8 cm. to the right of the mid-sternal line. There was tympany in Traube's space, the dullness reaching only to the fifth rib. It was thought at first to be an encapsulated tuberculous pleurisy, but aspiration showed a purulent fluid in which polymorphonuclear cells formed ninety-four per cent of the total cells. A rib was removed from the back and the cavity was drained. The patient is now in good condition. Sailer, after an examination of the literature, found ninety-five cases of pulsating empyema reported. Among the earliest reports are the three cases reported in 1840 by MacDonnell, of Montreal, and the cases by Stokes, of Dublin. Twelve of the ninety-five cases were serous effusions. The probable explanation of the pulsation is that ordinarily the elasticity of the lung takes up the pulsation, but if the lung be held firmly by adhesions or is completely compressed, the pulsating waves are entirely spent upon the chest wall. To pulsate, the fluid must always be under high pressure.

Cystic Kidney. DR. R. I. COLE.

Male; 41 years; complains of pain, shortness of breath, and weakness in back. He did not know date of onset. Fifteen years ago after rowing he noticed an enlargement of his abdomen, but it gave him no discomfort. Eight years ago a physician told him he had albumin in his urine. Two years ago his color changed; he became cyanosed, and there was pigmentation over his forehead and cheeks. On admission to the hospital he showed some cyanosis, a moderate grade of arteriosclerosis, and signs of cardiac weakness, but no heart murmurs. His abdomen was distended with distinct bulging in the flanks. As soon as the ascites had decreased a large mass was made out in the left flank, deep in the abdomen. It can be lifted forward from behind and has an irregular surface with prominences, one of which resembles a ball three or four cm. in diameter. On the right side in a similar position is a like tumor reaching down into the pelvis. It is far back in the abdomen and can be lifted forward. It also has irregularities. The patient shows symptoms of cystic kidneys. He has signs of cardiac weakness; urine of low specific gravity; some albumin and casts. While in the hospital the swelling of his legs and ascites disappeared and his shortness of breath improved. Up to this time he had never had blood in his urine, but a few days after his discharge from the hospital he returned with a specimen of bloody urine which he had passed. The patient also shows a pigmentation over forehead and cheeks in addition to the cyanosis which is constantly present. His hæmaturia may be due to rupture of small vessels between the cyst walls. The symptoms which give reason for the diagnosis of cystic kidneys are, large bilateral tumors, cardiac weakness, chronic nephritis, and hæmaturia. Three of Dr. Osler's four cases were recognized during life.

Congenital Cystic Kidney. DR. C. H. BUNTING.

The term cystic kidney denotes the same as the large polycystic kidney of the French. The first cystic kidney reported was at the Royal Society in Paris before 1725. The first congenital cystic kidney was reported before 1790. The last summary made in 1900 gives two hundred cases in adults, ninety of which were congenital, and thirteen were in infants. Cystic kidney occurs in about the same proportion in each sex, and may be found at all ages from the premature, or still-born, infant to old age. There is a remarkable family tendency. Virchow reports cases in which four of six children were affected. Singer reports a family in which the first, fourth, seventh, tenth, and thirteenth children had bilateral cystic kidneys, the other children being normal. The condition also appears in the second generation. But a single case of crossed inheritance is reported, the inheritance in all the others being from father to son or from mother to daughter. The kidneys of the new-born may be very large, cases being reported in which the pair weighed over a thou-

sand grams. In the adult they have been found weighing over five thousand grams.

Dr. Bunting passed about sections from gross specimens from the liver and kidneys obtained at autopsy of two children of the same mother. In the cortex of these were fine cysts. In the liver the portal surfaces had the appearance of an oak leaf. Through the medulla there was marked dilatation of the ducts, some of them divided up into finger-like processes. There were also mitotic figures present. In the liver there was increase in the size and number of the bile ducts. Cystic liver occurs in 20 per cent of the cases of cystic kidney. In the adult these cysts are lined with flattened epithelium and have a fluid content but no connection with the bile ducts. The theories of formation of cystic kidneys are grouped under four heads—the obstruction theory, new-growth theory, a theory of malformation in the development, and a theory which places them between malformation and new growth, and is a combination of the two. Virchow believed at first in the obstruction theory. In 1875 an advocate of the new-growth theory claimed that there were outgrowths from the tubules which were solid or tubular and underwent a colloid degeneration, and analogous to adenocystomata of the ovaries. The malformation theory dates from Kussner, who thought the condition to be due to a failure of the collecting tubules to open into the pelvis. The advocates of the fourth theory believed that the condition arose from the failure of the undifferentiated epithelium to grow in equilibrium. The lesions are ones of epithelial hyperplasia, which would not be included among new growths; they are adenocystomata. The ducts in the pancreas and liver show the same hyperplastic condition. These cases can show malformation in other parts. Polydactylism, hydrocephalus, harelip, atresia of anus or vagina, recto-vesical fistulæ, heart lesions, patent Ductus Botalli, and many associated defects in the genito-urinary organs have been found in these cases. The lesion is more nearly related to congenital malformation than to new growth, and we must look in the parents for the cause. Only ten per cent of cases are unilateral. Cystic kidneys may be found in all ages from infants to adults of eighty years. As a rule if there is enough cortex for the person to live for awhile after birth he may live a normal lifetime unless cut off by chronic nephritis. In adults with cystic kidneys there are the same associated malformations and liver conditions. It is very difficult in the adult kidney to make out anything in regard to the pathogenesis or histogenesis on account of the great changes that have taken place.

Infectious Arthritis. Dr. R. Fayerweather.

A report was made of bacteriological work carried out by him in the laboratory of the Tufts College Medical School, Boston. Of nine cases of various clinical types, four yielded positive bacteriological results. In the positive cases two clinical types are represented—one being a case of typical articular rheumatism; the others clinically infectious in character, being of the variety designated by Schüller *polyarthritis chronica villosa.* Operation was performed in two of the latter cases, and cultures taken from the joint-fluid and from the excised synovial villi. In the other cases the fluid was aspirated under rigid aseptic precautions. All inoculations were made on blood serum and pure cultures obtained in every instance. In the case of acute rheumatic fever the same organism was obtained from each knee-joint. In the operative cases the organisms cultivated were also demonstrated alone in stained sections of the excised villi. The clinical and pathological reproduction of the lesions was accomplished in rabbits by intra-articular injection of small doses of the cultures in bouillon suspensions. In one case the organisms were identified in the lesions, as in the human tissue. Large intravenous doses were without effect. The organisms found in these four cases could not be identified with any described in the various manuals. Three are bacilli of a spore-bearing variety, but with distinct differences in their cultural peculiarities; one is chromogenic. Of these, that isolated from the case of acute articular rheumatism is one. The fourth is a small diplobacillus, non-sporing, bearing only a slight resemblance to the pneumococcus. The clinical and pathological characteristics of polyarthritis chronica villosa were emphasized, and their distinction from acute articular rheumatism and the progressive form of arthritis deformans pointed out. The bacteriological work of others in this particular field was briefly referred to. The sum total of evidence is for a varied rather than a specific microbic etiology. Cultures were shown of the organisms here reported, also microscopic preparations showing their presence in the actual lesions.

THE JOHNS HOPKINS HOSPITAL HISTORICAL CLUB

October 16, 1905.

Dr. MacCallum in the chair.

John Howard's Observations on Hospitals (1773-1790). Dr. Hurd.

Two books have been added recently to the library of the Nurses' Training School of the Johns Hopkins Hospital, the first entitled the *"State of the Prisons in England and Wales with Preliminary Observations and an Account of Some Foreign Prisons and Hospitals,"* and the second, published in 1789, a few months before Howard's death, entitled *"An Account of the Principal Lazarettos in Europe with Various Papers Relative to the Plague; Together with Further Observations on Some Foreign Prisons and Hospitals and Additional Remarks on the Present State of Those in Great Britain and Ireland."* These, together with a copy of the *"Life of John Howard,"* by J. B. Brown, which had also been added to the same library, were shown. It is evident that Howard's interest in hospital reform was excited by the work which he had undertaken in connection with jails and prisons. He found prison infirmaries in shocking hygienic condition with a moral atmosphere which was most detrimental to all inmates. He consequently began to visit infirmaries, poor-houses, orphan asylums, lazarettos and hospitals, as well as prisons and jails wherever he went, and the volumes men-

tioned contain full and interesting details of these visits. He investigated thoroughly, setting down his conclusions without prejudice, but often with startling frankness, and accumulated a mass of facts which moved good men in every country to reform all penal and charitable institutions. It would be interesting to give many of the details contained in the two volumes, but I will content myself with a brief account, in his own words, of what he found in the London hospitals. He says:

"I shall beg leave to subjoin a few general observations concerning defects in the London hospitals, premising that I fear the public attention to them is much relaxed of late years in consequence of the newer establishment of dispensaries which have multiplied so as to injure the funds of the older institutions.

"The securities and fees required at admission into many of the hospitals bear hard upon the poor and absolutely exclude many of those who have the greatest occasion for charitable relief. The nurses' fees, in particular, open a door to many impositions.

"The visits of Governors are too often only a matter of form, the visitor hurrying out of an offensive room and readily acquiescing in the reports of nurses, etc. Hence I apprehend many instances of neglect in surgeons and their dressers as well as other officers go unnoticed.

"I have never found any clergyman administering consolation and admonition to the sick; and prayers are usually attended by very few.

"White-washing the wards is seldom or never practised, and injurious prejudices against washing floors and admitting fresh air are suffered to operate.

"Bathing, hot or cold, is scarcely ever used; I suppose because it would give trouble to the attendants. There are no convalescent or sitting rooms so that patients are often turned out very unfit for work or the common mode of living.

"The admission of great quantities of beer for patients from ale-houses by alleged or pretended orders from the faculty is a great and growing evil. Every proper article of diet should be provided by the hospital and no other on any account be admitted.

"It is a pity that for want of attention to these circumstances, such noble institutions should be rendered of much less public utility than was intended by their governors, founders, and supporters."

In some of the accompanying notes interesting side-lights are thrown upon usages which to us seem incredible. Thus, for example, he speaks of the urine of the patients in one hospital being sold as a perquisite of the nurses. In another hospital patients were found lying in loose straw upon the floor. In a third (this was in Ireland) the bath house had been converted into a pig-pen and sheltered the pigs belonging to the warden of the hospital. In still another, two patients were found lying in the bath-tub for the lack of any other bed.

As a result of his observations and investigations he presents the following summary of what he regards as the desiderata of a good hospital:

"The situation of an Infirmary or Hospital should be on elevated ground, near a stream of water, and out of a town. The wards, if only one for each sex, to be twenty-five to thirty feet high, arched and without apartments over them; otherwise, the building to consist of only two stories besides the cellars, and the area extended as far as necessary upon this plan, that the inconvenience of higher rooms may be avoided. The first floor raised four or five steps from the ground and the ascent made easy to the entrances. The wards fifteen feet high to the ceilings and distinct ones for medical and chirurgical patients. Two doors to each ward, one of them iron or latticed or canvas. Staircases of stone, spacious, convenient and easy as in Italy, Marseilles, Malta, etc. No room to contain more than eight beds. The windows lofty and opposite, or circular apertures (as at Leeds infirmary), opening into passages not less than six feet wide; hasps and staples to the upper sashes to prevent their being shut at improper times, or like those at Guy's hospital: a stone gallery for more readily opening and shutting the windows as in the Italian hospitals. The ceilings lathed and plastered and proper apertures in them. The fire-places in the middle of the longer side of the wards; the beds in spacious recesses as at Toledo or Burgos; or to each bed a recess with curtains as at Genoa, Savona, etc. The bedsteads iron, painted and with a screw that the backs may be easily raised, or lowered; the beds on varnished boards or laths, with hair mattresses. In each ward a cistern, basin and towel for the patients. Vaults on the outside of the wards and water-closets as at Guy's hospital; for every improvement that may render such places less offensive should be carefully adopted in all houses containing a number of inhabitants. Airy rooms and refectories for convalescent patients; one spare and unfurnished ward; each ward to be taken in succession and called the spare ward. The kitchen, washhouse, brew-house, and bake-house out of the house, but if the kitchen be in the house it should be lofty as in Christ's hospital (not underground), and the entrance through the servants' hall. A convenient bath with an easy descent into it. A piazza and spacious walk to induce patients to take the air and exercise. The wards washed once each week—scraped and lime-whited at least once a year. (The machines at Northwich for supplying the salt-mines with fresh air, being on a simple construction, would be of admirable use in hospitals, especially if situated in confined places.) The patients washed at their admission in the cold or warm bath and to conform strictly to the rules of nicety and cleanliness."

History of Typhoid Fever. DR. MCCRAE.

One of the important lessons in this is the difficulty which may attend the recognition of a disease. In early times typhus fever, the plague, malarial fevers, relapsing fever, and typhoid fever were more or less grouped together, but the greatest difficulty came in the separation of typhus from typhoid fever. It is not possible to recognize typhoid fever in the description in Hippocrates and Galen, although it is possible that the disease described as hemitertian was typhoid fever. Certain writers gave descriptions of a condition which suggests that they had seen typhoid fever and recognized some of its essential features. Spigelius, Sydenham, Hoffman, Struthers, and Gilchrist were among these, while Morgagni described a case in considerable detail. In the early part of the nineteenth century through more careful work in pathological anatomy it was recognized that in a certain group of cases with continued fever there were intestinal lesions. In 1829, Louis described a disease to which he gave the name of typhoid fever, but it is doubtful if he made a clear distinction between it and typhus fever. At this time the prevailing disease in France was typhoid, while elsewhere on the Continent and in England typhoid and typhus fevers existed together. The general opinion was that the group of these cases was associated with intestinal lesions. It is to Gerhard, of Philadelphia, that the

greatest credit for the clear distinction is due. He studied under Louis in Paris, and on his return to Philadelphia saw cases of typhoid fever, but we cannot be certain that he recognized clearly the distinction between it and typhus fever until the epidemic of the latter disease in 1836. He was then able to set forth clearly the distinction between the two diseases in his report in 1837. Stillé, Shattuck, James Jackson, Sr., and Hall were all early supporters of the duality of the diseases. In 1824 Nathan Smith wrote a treatise in which he gave a very clear description of the features of typhoid fever, although he may not have recognized its distinction from typhus fever. In 1842, Elisha Bartlett published the first book in which the two diseases were discussed separately. There were many who accepted the new views at once, among them being especially Jenner and Murchison in England and Griesinger in Germany.

After the recognition of the disease there were many conjectures as to its mode of origin. Murchison was the first to suggest that the excreta were the source of infection, but for a time special emphasis was laid on putrefaction. One of the first men who held clear ideas on the question of infection was Budd, who lived in Bristol. His articles in the Lancet from 1856 to 1860 are well worth reading. He believed that the danger was in the stools, that infection arose from a definite source, and could not arise *de novo*. The discovery of the causal bacillus in 1880 by Eberth and since then the large amount of work done on the various problems have widened our knowledge of the disease and the problems connected with it.

Discussion.—Dr. Welch pointed out that it was impossible to distinguish the two diseases until autopsies were carefully made. As a result of these we find a considerable number of descriptions of lesions which are undoubtedly of typhoid fever. He drew attention to the excellence of the description of typhoid fever given by Nathan Smith, one which had not been approached up to his time and hardly surpassed since. The French writers of the early nineteenth century, particularly Broussais, held that all fevers were symptomatic. No name holds so prominent a place in establishing the distinction between the two diseases as that of Gerhard. His conclusions were reached by seeing the diseases separately. In Dublin, Graves and Stokes held out so long because they saw the two diseases together.

Dr. W. G. MacCallum drew special attention to the accurate description given by Budd, and pointed out that he was one of the first to describe amœbic dysentery. He also emphasized the value of Hoffman's work on the pathological anatomy of typhoid fever.

NOTES ON NEW BOOKS.

Diseases of the Blood. By Prof. Dr. P. Ehrlich, Prof. K. Von Noorden, Dr. A. Lazarus and Dr. F. Pinkus. *Nothnagel's Encyclopedia of Practical Medicine.* American Edition. (*London and Philadelphia: W. B. Saunders & Co., 1905.*)

This authorized translation under the direct supervision and editorship of Alfred Stengel makes accessible to English readers the excellent work of the Ehrlich school of hæmatology on the blood and its diseases. While the original has been faithfully reproduced, the editor has improved on the original by interpolating the views of opponents on mooted questions in hæmatology. These insertions are most noticeable in the chapter on the histology of the blood, and in the section on pseudoleukæmia (Hodgkins disease), where full notice is given of the excellent work of the American investigators of this subject, Reed, Simmons, and Longcope. This chapter has been further enhanced by the reproduction of the plates from Longcope's monograph on the subject. The editor has further brought the book up to date by the addition of notes on the various subjects treated, from the literature subsequent to the appearance of the original German edition. Among such additions is a review of the subject of X-ray treatment of leukæmia.

The work as a whole is to be highly recommended to all interested in hæmatology.

Atonia Gastrica (*Abdominal Relaxation*). By Achilles Rose, M. D., and Robert Coleman Kemp, M. D. 12mo. pp. 204. (*New York and London: Funk & Wagnalls Company, 1905.*)

This monogr h gives an exhaustive résumé of the nomenclature, history, diagnosis, and treatment of gastric atony. A third of the volume is devoted to the methods of outlining the stomach, accompanied by tables and diagrams. All the newer methods, including the use of the gastro-diaphane, the Röntgen ray, and the stomach whistle devised by one of the authors, are fully described.

A discussion of the treatment of gastric atony by the author's method of support with adhesive strapping and the application of such strapping to other types of abdominal ptosis, together with the report of cases, conclude the volume. T. R. B.

Manual of the Diseases of the Eye. For Students and General Practitioners. By Charles H. May, M. D., Ophthalmic Surgeon to the City Hospitals, Randall's Island, New York. Fourth edition, revised. With 360 original illustrations, including 21 plates, with 60 colored figures. (*New York: William Wood & Co., 1905.*)

This is the fourth edition of May's Manual of the Diseases of the Eye. The author has carefully gone over the text and corrected a few errors which were present in previous editions. The work has been enriched with a number of additional color plates, and we are glad to note the addition, also, of several new illustrations, especially those to the subject matter of lid operations. The general arrangement of the book is very good, and the essentials of ophthalmology are set forth in a clear, accurate, and sufficiently full manner as to admirably serve the needs of the medical student, for whose use the book is designed, in his course in ophthalmology. B. B. B., Jr.

Color-Vision and Color-Blindness. A Practical Manual for Railroad Surgeons. By J. Ellis Jennings, M. D., Professor of Diseases of the Eye, Medical Department, Barnes University, St. Louis. Second edition, thoroughly revised, with illustrations. (*Philadelphia: F. A. Davis Company, 1905.*)

This is the second edition of Jennings' book on Color-Blindness. The author does not aim at any originality in the book, but gives an excellent résumé of the history of color-blindness, the various well-known theories as to the development of color sensation, and the usual methods of determining the existence of partial and complete color-blindness. We are glad to note in this edition a good description of the Williams and Thomson lanterns, which are not used as frequently as they should be by ophthalmologists, even when requested to report on the presence or ab-

sence of color-blindness. We know of no work on this subject which is more compact and valuable from a practical standpoint, and we recommend its perusal to all those who are accustomed to examining the eyes of railroad employes and applicants for the army, navy, or other branches of the public service. B. B. B. Jr.

Biographic Clinics. Volume III. Essays concerning the influence of visual function, pathologic and physiologic, upon the health of patients. By GEORGE M. GOULD, M. D., Editor of American Medicine, etc. (*Philadelphia: P. Blakiston's Son & Co., 1905.*)

This attractive book is the third in Dr. Gould's series, and, like its predecessors, it preaches the gospel of the new ophthalmology and illustrates the precept by the examples of John Addington Symonds and Henri Taine, gleaned from their biographies and correspondence. The doctrine is also enforced by the republication of "Eyestrain as a Cause of Headache and Other Neuroses," by Simon Snell, of Sheffield, England, and "Slight Errors of Refraction and their Influence on the Nervous System," by C. Ernest Pronger, of Harrowgate, England. It contains, in addition, the interesting papers which the author has contributed to medical and scientific journals during the past two years on subjects allied to the main topic of the book. The chapter entitled "Optic and Ocular Factors in the Etiology of the Scoliosis of School Children" is most valuable and suggestive, and should be as thoroughly considered by orthopedic surgeons as by ophthalmologists. The same is true of the chapter, "Pathologic Results of Dextrocularity and Sinistrocularity," which in many cases seems to explain the etiology of scoliosis and head-tilting. A chapter on the "Reception of Medical Discoveries" also furnishes interesting and stimulating reading, although the reader doubtless will feel that its tone is too bitter and pessimistic. The author is so much in earnest he has little regard for conservatism and is impatient of criticism. The book as a whole is most suggestive and valuable.

Dispensing Made Easy. With numerous formulæ and practical hints to secure simplicity, rapidity, and economy. By WM. G. SUTHERLAND, M. D. Aberd. Second edition, revised. (*Bristol: John Wright & Co.; London: Simpkin, Marshall, Hamilton, Kent & Co., Ltd., 1905.*)

This little manual is for English practitioners in England. All references are to the English authorities. The formulæ are good and the practical directions are clear and judicious. An American adaptation with references to the U. S. Pharmacopœia would render it equally useful on this side of the Atlantic.

Medical and Surgical Reports of the Bellevue and Allied Hospitals in the City of New York. Volume I, 1904. Edited by ALEXANDER LAMBERT, M. D., W. K. DRAPER, M. D., and GEORGE WOOLSEY, M. D.

This is a pleasing volume typographically, with clear type, broad margins, and good paper. The full and complete account given of the system of taking and preserving histories will prove of much advantage to other hospitals. One cannot avoid an expression of surprise, however, that *entries* in copying ink in the case record are contemplated. Those who have had an experience with the stickiness of copying ink and the ease with which the page becomes blurred and disfigured, can but deprecate its use. Paper histories for dispensary patients also seem too fragile for ordinary use. These are minor criticisms, however. The index of diseases and complications seems admirably planned and the effect of this excellent system must be to render all case histories very accessible.

The papers which follow are of varying excellence. Lambert's "Some Statistics and Studies from the Alcoholic Wards of Bellevue Hospital," Gilman Thompson's "Report of Fourteen Cases of Pernicious Anemia," and Luckett's "Rational Treatment of Tetanus" are excellent scientific papers. Others like "Prevention of Shock During Surgical Operations," "Observations on Some of the Molecular Changes Caused by Light," seem rather popular than scientific. There are some typographical errors, as Halstead for *Halsted*, anthropathies for *arthropathies*.

International Clinics. Vol. II. Fifteenth Series. 1905. (*Philadelphia and London: J. B. Lippincott Company, 1905.*)

The present volume is fully equal to the previous volumes of this publication. The articles, as might be anticipated from the manner of collection, are of unequal excellence. D. Barty King's "Observations on the Treatment of Pulmonary Hemorrhage by Adrenalin Chlorid", is a careful and systematic account of the reasons why adrenalin chlorid is contra-indicated in the treatment of hæmoptysis. The same is true of Edes' "Suggestions Regarding the Treatment of Neurasthenia," which is equally a careful statement of the result of long experience and much observation. Willson's "Diagnosis of Incipient Pulmonary Tuberculosis" is a timely paper, full of accurate observation of eighty-six cases of incipient or advanced tuberculosis. His conclusion that "a positive diagnosis of tuberculosis should often be made long before fever is present and long before tubercle bacilli have been found," commends itself to all who have given attention to the subject. Others, like Hemmeter's "Physiologic Aspects of Ehrlich's Side-chain Theory and its Application to the Physiology of digestion," seem more theoretical than practical.

Taken as a whole, however, the volume is full of interest and deserves a careful reading on the part of those who are engaged in the practice of medicine.

Natural Science in Hygiene, or The Life-History of the Non-Bacterial Parasites Affecting Man. For the use of students of Public Health. By JAMES RODGER WALTON, M. A., B. Sc., M. D., Diplomate in Public Health, University of Cambridge. (*Bristol: John Wright & Co.; London: Simpkin, Marshall, Hamilton, Kent & Co., Ltd., 1905.*)

This is a very elementary manual of the life-history of the parasites of the vegetable kingdom, such as fission fungi, yeast fungi, and mould fungi; also of protozoa, vermes, insecta, and arachnida, parasites of the animal kingdom. The author confines himself to those parasites which affect man and of necessity the view which is given is wholly practical. It is a convenient book and serves a good purpose by collecting together many otherwise isolated facts. It should lead the reader to investigate these animal and vegetable parasites more fully and to read more ambitious works.

The Medical Epitome Series. Practice of Medicine. A manual for students and practitioners. By HUGHES DAYTON, M. D. Series edited by VICTOR COX PEDERSEN, A. M., M. D. (*New York and Philadelphia: Lea, Brothers & Co., 1905.*)

This is an admirable little manual. Its descriptions of disease are clear and concise. The material is systematically arranged and the treatment of disease suggested is modern.

Chirurgie du système nerveux (Crâne et encéphale. Rachis et moelle. Nerfs). GEORGES MARION, professeur agrégé à la Faculté de médecine de. (*Paris: G. Steinheil, éditeur.*)

The appearance of this volume is most timely, dealing as it does with a subject that is attracting rapidly increasing attention. The work is extensive and one is struck with the value of the numerous illustrations, which are clear and true.

The first of the three parts, dealing with the skull and its contents, opens with an excellent chapter on the topographical anatomy and the methods of localizing the situations of the various intracranial structures and regions, which is followed by a carefully prepared chapter on the technique of cranial operations. Then follow a number of chapters in which are considered the indications for and the treatment in affections of the skull and brain, including, among others, injuries, intracranial hæmorrhage, traumatic epilepsy, and new growths. The chapter dealing with the localization of and extraction of foreign bodies from within the cranium is of particular interest.

Part two is devoted to the surgical diseases of the vertebræ and spinal cord, a thorough presentation of the topographical anatomy being followed by a consideration of the operative procedures. Lastly are considered various affections—trauma, infections, new growths—demanding surgical treatment.

Part three is devoted to the surgery of nerves. Conditions, such as compression, rupture, and tumors, which demand surgical measures are first considered; then follow discussions of the operations for section, resection, elongation, suture, etc. The surgery of the sympathetic system is more briefly considered, though the section contains much of interest.

The descriptions of the operations throughout are clear and concise, and important features are brought out in an excellent manner both by the text and illustrations. There can be little doubt that this work contains the most complete presentation of the surgery of the nervous system that we have.

Psychiatry. A Text-book for Students and Physicians. By Stewart Paton, M. D. (*Philadelphia and London: J. B. Lippincott Company, 1905.*)

This work represents not only a new and timely text-book of psychiatry, but what is more important, offers a readable presentation of modern scientific conceptions regarding abnormal functioning of the brain. In a certain sense it may be regarded as a pioneer work in English. Three striking characters, and at the same time merits, may at once be indicated:

(1) The author throws out many of the dogmatic time-honored definitions of psychic anomalies which cumber treatises on mental disease, and which have been largely the outgrowth of incomplete observation and analysis of cases.

(2) He attempts to indicate some of the more conspicuous needs and means of approach in the scientific study and treatment of cases of alienation.

(3) He brings together in condensed form a mass of observations and opinions of current authors, particularly German, dealing with all phases of the subject.

Until comparatively recently the majority of English and American writers, following the example of Krafft-Ebing, have been content with psychiatry as a descriptive science and have offered simple symptomatic narratives of disease conditions. In 1885 a prominent American alienist, discussing the classification of insanity, said:

"It assumes three fundamental forms—*mania*, manifested by delusions of excitement, expansive ideas, exaggerations, self-consequence, incoherence, etc.; *melancholia*, manifested by delusions of depressing character, painful ideas, and apprehensions; *dementia*, representing conditions of mental failure and feebleness of mental action. All cases of insanity come under these three heads. Cases may be acute, sub-acute, chronic, periodic, paroxysmal, but they are either mania, melancholia, or dementia."

This ancient scheme with slight modification or amplification has also been found sufficient by many alienists and directors of insane hospitals even up to the present day.

Paton's book offers a grateful contrast to the older methods and doctrines, it points out that the actual number of demonstrated facts is relatively small in comparison with the mass of speculative hypotheses which have been accepted, from time to time, in lieu of facts, and emphasizes particularly the importance of the method which does not adopt uncritically inherited teachings but rather seeks to prove the ground inch by inch.

To the student who is looking for cut-and-dried statements this book will not appeal. On many questions the various possibilities are discussed, and opinions of different observers are set forth, but the conclusion is left undrawn. This from the didactic viewpoint would often seem unfortunate, but it is withal the safer part and more to be commended than the drawing of conclusions from insufficient evidence—a fault into which psychiatric writers are only too liable to fall.

Paton takes legitimate exception both to the methods of modern education which assemble a heterogeneous mass of humanity and subject all indiscriminately to an educational routine to which all are by no means equally adapted; likewise to the fanatic zeal of sociologic faddists in their efforts to "elevate the masses," and thus wrench them out of the conditions to which they were born, and in which they are calculated, by their mental and physical makeup to lead their lives. In the consideration of both these questions he sees important indications in the hitherto little-heeded subject—the prophylaxis of insanity. Speaking of the fallacies of so-called education Paton observes (page 9):

"Every one admits that it is the duty of the physician to warn those with weak hearts or lungs not to overtax those organs. Is it not equally important that the mental welfare of a community be safeguarded? Only some men are born to be educated; how many more, unfortunately, have thrust upon them an education which is disastrous not only to themselves, but also to the community at large. To prevent the sins of overeducated fathers and mothers from being visited upon the children unto the third and fourth generation is a problem of great sociological as well as economic importance to the state."

Further (page 198), "If the aid of intelligent physicians were sought in determining the question as to what children were fitted to receive a public school education, unquestionably many cases of insanity which develop later in life would never occur. It is a curious comment upon popular government that so little effort is being made along these lines, and that, while the public has the right to prevent the spread of measles or scarlet fever, it assumes no authority in matters relating to the prevention of alienation. . . . To render it possible for an individual who is physically and mentally unfitted for the stress associated with the effort to undertake the acquirement of what is termed a liberal education should be regarded as an offense against the public health and morality no less culpable than if one were to deliberately place him in an environment where he is exposed to an infectious disease."

The one urgent need of the immediate future in American psychiatry is an institution, hitherto quite unknown on this side, but whose advantages Europe has long enjoyed, namely, the University Psychiatric Clinic. To the qualifications of the modern clinic a separate chapter is devoted (pages 167 to 177). As the best example of the up-to-date insane hospital may be mentioned the new institution at Munich, completed last year, which is a type of the best fruits of modern intelligence in the construction and arrangement of clinics for the insane, for the most advantageous study and treatment of patients, and the purposes of clinical instruction. This institution has recently been the subject of an elaborate monograph by the director, Prof. Kraepelin (Barth, 1905, 2M), and was also briefly described by Paton in Science for September 8, 1905.

Considering the enormous strides which have been made in all departments of mental medicine, particularly within very recent years, Paton's book of 600 pages may be considered a condensed

one; indeed the objection may possibly be raised that sometimes the discussions are too brief, that in his endeavor to give credit to a wide range of opinions without becoming bulky, the author assumes a degree of familiarity with the subject on the reader's part and often forces him to some wholesome mental exercise in the way of reading between the lines.

The first part of the book, comprising 230 pages, is devoted to general considerations, including the more essential known facts in etiology, symptomatology, and treatment; the remainder of the book is given to the clinical description of disease-groups. In his scheme of classification Paton follows the "clinical" method, and he deals with the subject under the following heads:

(1) *Mental anomalies the result of defective development of the central nervous system.*

(2) *Psychoses which are probably in part the result of autointoxication.*

(3) *Psychoses the result of chronic intoxications.*

(4) *Psychoses associated with imperfect functioning of the thyroid gland.*

(5) *The manic-depressive group.*

(6) *The dementia præcox group.*

(7) *The dementia paralytica group.*

(8) *The epilepsy group.*

(9) *The hysteria group.*

(10) *Neurasthenic and psychasthenic states.*

(11) *Psychoses associated with organic disease of the central nervous system.*

(12) *The paranoia group.*

(13) *The senile group. Psychoses connected with the period of senile involution.*

Pleasantly conspicuous by their absence are the "symptomatic sub-groups" which exist in dozens in many text-books, and which are no more than names of isolated symptoms, if not indeed of mere surface appearances, which are thus assumed to represent disease varieties.

The treatment in general is a conservative one, the maniaco-depressive and dementia præcox groups are designated as provisional differentiations, which have been made, however, on principles "which are consistent with and not antagonistic to progress." The old epochal psychoses have been eliminated and in their places are discussed the predilection of certain pathologic mental conditions for certain periods of life, as well as the influence of the age of the patient in modifying the clinical manifestations in any given disease form.

The criticism may be made that the work is not pre-eminently adapted to the needs of the student who is totally unfamiliar with the subject and who is anxious for categoric statements and final facts. To the student, however, who is trained from the beginning to methods of research, and who esteems the process of personal investigation and careful analysis, of weighing opinions, and of tentative conclusion, above the acquiring of information by way of didactic dogmatism, an exposition of mental diseases such as the one under consideration will prove a wholesome guide.

CLARENCE B. FARRAR.

A Text-book of Physiology, Normal and Pathological. For Students and Practitioners of Medicine. By WINFIELD S. HALL, PH. D. (Leipzig), M. D. (Leipzig), Professor of Physiology, Northwestern University Medical School, Chicago. Second edition, revised and enlarged. Illustrated with 340 engravings and three colored plates. (*Philadelphia and New York: Lea Brothers & Co., 1905.*)

In this comprehensive work the author has endeavored to present as concisely as possible, not only physiology properly so-called, but such parts of allied subjects as might be considered useful in throwing light upon the central theme. Consequently one finds scattered throughout the book chapters or paragraphs relating to chemistry and physics, embryology and anatomy, pharmacology and pathology, clinical microscopy and clinical medicine; nor does the historical aspect of the subject fail to receive a passing word.

In order to present this vast amount of material within the compass of 800 pages (containing many illustrations), the author has been obliged to employ the greatest possible brevity. This fact not only renders the book very unattractive reading—in which respect it differs but little from the majority of text-books—but often places the sense a little beyond the grasp of the student who is approaching the subject for the first time. Moreover a condensation which necessitates the allotment of but six lines to the Young-Helmholtz theory of color-vision, one-half page to color-blindness, three-quarters of a page to the splanchnic nervous system, three pages to the vasomotors and so forth, is not likely to give the beginner a very clear conception of the subjects in question.

If the work be regarded as a compend, that is, an aid to the student in reviewing before examination, then its size and the diversity of the material which it contains may somewhat impair its usefulness, while viewed as a dictionary of the medical sciences, it may be a little incomplete and lacks the convenience of an alphabetical arrangement.

The author is a teacher of some experience and the publication of this second edition is doubtless the response to a demand, and there is every reason to believe that where this demand exists the work will meet with the approval of teachers of physiology, especially as it is apparently up to date and contains much valuable information.

INDEX TO VOLUME XVI OF THE JOHNS HOPKINS HOSPITAL BULLETIN.

Abnormalities in the form of the kidney and ureter dependent on the development of the renal bud, 51.
Accessory and twisted omentum, 401.
Agglutination reactions of the Bacillus dysenteriæ (Shiga) with the blood serum of patients suffering with summer diarrhea, report upon, 93.
Amick, A. L., and Stokes, W. R., Typhoid appendicitis without other intestinal lesions, 284.
Anatomical laboratory of the University of California, 32.
Anatomical material—its collection and its preservation at the Johns Hopkins Anatomical Laboratory, 38.
Anemia, aplastic, associated with lymphoid hyperplasia of the bone-marrow, 127.
Anemia, pernicious, etiology and pathogenesis of, 222.
Aneurysm, aortic, unusually large, 331.
Announcement concerning graduate instruction in the Medical Department of the Johns Hopkins University, 70.
Bacillus aërogenes capsulatus in puerperal infection, 136.
Bacillus dysenteriæ (Shiga), agglutination reactions of, with the blood serum of patients suffering with summer diarrhea, 93.
Bacillus violaceus Manilæ, 89.
Baer, W. S., and Kennard, H. W., The diagnostic value of tuberculin in orthopedic surgery, 13.
Barker's Manual, teaching of anatomy as illustrated by, 29.
Bile, effect of, upon the ester-splitting action of pancreatic juice, 20.
Birge, E. G., Some observations on the occurrence of Micrococcus zymogenes, 309.
Blood-vessels, partial occlusion of, especially of the abdominal aorta, 346.

Blumer, G., Aplastic anemia associated with lymphoid hyperplasia of the bone-marrow, 127.
Books received, 26, 204, 312.
Bowley, R. L., and Clark, A. H., A case of Cæsarean section following ventral fixation, 101.
Brachial artery, high bifurcation of, with reunion at the elbow, 65.
Brem, W. V., Action of the toxic agent of lobar pneumonia: Therapeutics, 321.
Briggs, J. B., Recurring phlebitis of obscure origin, 228.
Bunting, C. H., The etiology and pathogenesis of pernicious anemia, 222.
Cæsarean section following ventral fixation, case of, 101.
Calvert, W. J., A convenient still to make absolute alcohol, 68; A practical method of demonstration, 19; Movability of the heart in pneumothorax, 300.
Cancer in mice (adeno-carcinoma, Jensen), development of, 130.
Carcinoma of the prostate, early diagnosis and radical cure of, 315.
Carcinoma, primary, of the right Fallopian tube, 397.
Cardiograms obtained from a case of operative defect in the chest wall, 394.
Chatard, J. A., Acute pericarditis complicating acute lobar pneumonia, 334.
Christian, H. A., Some newer aspects of the pathology of fat and fatty degeneration, 1.
Churchman, J. W., A case of congenital urethral stricture associated with hematuria and symptoms suggesting renal disease, 256.
Circulation of the blood, history of—contributions of the Italian anatomists and physiologists—their bearing upon the discovery by Harvey, 165.
Clark, A. H., and Bowley, R. L., A case of Cæsarean section following ventral fixation, 101.
Clarke, T. W., Repeated copious hemoptysis from an aortic aneurism, extending into the right lung and finally rupturing into the pleura, 98.
Clowes, G. H. A., Preliminary communication regarding an immune body capable of inhibiting the development of cancer in mice (adeno-carcinoma, Jensen), 130.
Comparative surgery, 179.
Cordell, E. F., Dr. Charles Frederick Wiesenthal's medical reports, 407; Dr. Heinrich or Henry Keerl, of Baltimore, the "Hessian Surgeon," 133.
Cornell, W. B., Infantile paralysis of the abdominal muscles, with report of a case, 11.
Correspondence: Dewis, J. W., Early autopsies at St. Croix Island, 199; Rose, A., Knowledge of Greek and corruption of language, 263.
Cotton Mather's rules of health, 293.
Crile, G. W., Surgical physiology, 269.
Cullen, T. S., Fibroma of the abdominal wall; Primary carcinoma of the right Fallopian tube; An accessory and twisted omentum, 397; Vaginal cysts, 207.
Cushing, H., The special field of neurological surgery, 77.
Cushing, H., and others, Comparative surgery, 179.
Cyst, acquired, of the conjunctiva containing an embryonic tooth-like structure, case of, 308.
Demonstration (of relation of organs), practical method of, 19.
Developmental relations of the kidney and ureter in human embryos, note on, 49.
Diagnostic value of tuberculin in orthopedic surgery, 13.
Diaphragmatic grooves on the liver, 364.
Discussion: Dr. Baer, Gonorrhœal exostoses of the calcaneus, 385; Dr. Briggs, Recurring phlebitis of obscure origin, 111;—Dr. Browne, Recurring phlebitis of obscure origin, 111;—Dr. Cole, Experimental streptococcus arthritis, 115;—Dr. Emerson, History of blood platelets, 201;—Dr. Finney, Peripancreatic abscess, 148;—Dr. Futcher, Adeno-carcinoma of the umbilicus, 110; Cancer of liver, 110;—Dr. Howell, Surgical physiology, 202;—Dr. MacCallum, Arteriovenous aneurism of the thigh, 119; Biliary cirrhosis of family type, 113;—History of typhoid fever, 414;—Dr. Osler, Arteriovenous aneurism of the thigh, 119; Typhoid fever showing some unusual features, 119;—Dr. Pancoast, Gastric ulcer, 118;—Dr. Welch, History of typhoid fever, 414; The immunization of mice to cancer, 146.
Endocarditis in tuberculosis, 303.
Erlanger, J., A report of some observations on heart-block in mammals, 234; Cardiograms obtained from a case of operative defect in the chest wall, 394.
Ester-splitting action of pancreatic juice, effect of bile upon, 20.
Fat and fatty degeneration, some newer aspects of the pathology of, 1.
Faure, J. D., The surgery of the posterior mediastinum; its past and its future, 125.
Fibroma of the abdominal wall, 397.
Fixation of tissues by injection into the arteries, 66.
Flechsig's investigations on the brain, 45.
Flint, J. M., The anatomical laboratory of the University of California, 32.
Freese, J. A., The force of contraction of the gall-bladder and the course of its motor and inhibitory nerve fibers, 235.
Gall-bladder, force of contraction of, and the course of its motor and inhibitory nerve fibers, 235.
Goitre, exophthalmic, pathological anatomy of, 287.
Grave robbing in England, development of, 42.
Halsted, W. S., The partial occlusion of blood-vessels, especially of the abdominal aorta, 346.
Harris, H., Renal decapsulation in nephritis, with report of a case, 404.
Heart-beat, rise of the present conceptions as to the cause of, 338, 377.
Heart-block in mammals, report of some observations on, 234.
Helmholz, H. F., and Little, H. M., Situs transversus and atresia of the pylorus, 249.
Hemiplegia, right-sided infantile, case of, 21.
Hemmeter, J. C., The history of the circulation of the blood—contributions of the Italian anatomists and physiologists—their bearing upon the discovery by Harvey, 165.
Hemoptysis from an aortic aneurism, extending into the right lung and finally rupturing into the pleura, 98.
Herrinton, Minerva, High bifurcation of the brachial artery with reunion at the elbow, 65.
Herter lectures: The contributions of pharmacology to physiology, 351, 389.
Hewlett, A. W., The effect of the bile upon the ester-splitting action of pancreatic juice, 20.
Hildanus, Fabricius Guilhelmus, the father of German surgery, 7.
Hill, E. C., On the first appearance of the renal artery, and the relative development of the kidneys and Wolffian bodies in pig embryos, 60.
History of the circulation of the blood, 165.
History of medicine in Maryland during the Revolution, contribution to, 241.
Hough, W. H., A case of unusually large aortic aneurysm, 331.
Howell, W. H., Announcement concerning graduate instruction in the Medical Department of the Johns Hopkins University, 70.
Hyperplasia of the chromophile cells of the hypophysis as the cause of acromegaly, with report of a case, 157.
Immune body capable of inhibiting the development of cancer in mice, 130.
Infantile paralysis of the abdominal muscles, with report of a case, 11.
Keerl, Dr. Heinrich or Henry, of Baltimore, the "Hessian Surgeon," 133.

Kennard, H. W., and Baer, W. S., The diagnostic value of tuberculin in orthopedic surgery, 13.
Kidney and ureter, abnormalities in the form of, dependent on the development of the renal bud, 51.
Kidney and ureter, developmental relations of, in human embryos, 49.
Lewis, D. D., Hyperplasia of the chromophile cells of the hypophysis as the cause of acromegaly, with report of a case, 157.
Little, H. M., The Bacillus ærogenes capsulatus in puerperal infection, 136.
Little, H. M., and Helmholz, H. F., Situs transversus and atresia of the pylorus, 249.
MacCallum, W. G., Marcello Malpighi, 1628-1694, 275; The pathological anatomy of exophthalmic goitre, 287; Tumor of the parathyroid gland, 87.
Mall, F. P., Anatomical material—its collection and its preservation at the Johns Hopkins Anatomical Laboratory, 38; On the teaching of anatomy as illustrated by Professor Barker's Manual, 29.
Malpighi, Marcello, 1628-1694, 275.
Marshall, H. T., Endocarditis in tuberculosis, 303.
Martin, E. G., The rise of the present conceptions as to the cause of the heart-beat: I. Early ideas and the myogenic theory, 338; II. The myogenic theory and modern studies of rhythmicity, 377.
Meyer, H., The contributions of pharmacology to physiology, 351, 389.
Micrococcus zymogenes, observations on the occurrence of, 309.
Miller, E. F., A multiplex slide-holding device, 132.
Miller, W. S., A needle and clamp for injecting lymphatics, 273.
Moody, R. O., Diaphragmatic grooves on the liver, 364.
Movability of the heart in pneumothorax, 300.
Multiplex slide-holding device, 132.
Myers, B. D., Fixation of tissues by injection into the arteries, 66.
Myogenic theory and modern studies of rhythmicity, 377.
Myogenic theory, early ideas and, 338.
Needle and clamp for injecting lymphatics, 273.
Nephritis, renal decapsulation in, 404.
Neurological surgery, special field of, 77.
Notes and news, 24.
Notes on new books, 25, 120, 150, 202, 239, 265, 289, 311, 347, 387, 414; American year-book of medicine and surgery: Medicine, 266; Surgery, 289;—Appleton's medical dictionary, 25;—Balfour, A., First report of the Wellcome Research Laboratories, 120;—Ball, J. M., Modern ophthalmology, 152;—Ball, M. V., Essentials of bacteriology, 290;—Barr, M. W., Mental defectives, their history, treatment, and training, 124;—Beebe, S. P., and Buxton, B. H., Outlines of physiological chemistry, 291;—Benedict, A. L., Practical dietetics, 203;—von Bergmann's System of practical surgery (vol. v), 311;—Bishop, S. S., Diseases of the nose, throat and ear, 124;—Blair, C., Errors of refraction and their treatment, 312;—Blake, E., The intestinal catarrhs, 347;—Böhm, A. A., and others, A text-book of human histology, 120;—Bolton, H. C., The follies of science at the Court of Rudolph II, 1576-1612, 239;—Brubaker, A. P., A text-book of human physiology, 120;—Burton-Fanning, F. W., The open-air treatment of pulmonary tuberculosis, 291;—Bryant, J. D., Operative surgery, 348;—Cattell, H. W., Post-mortem pathology, 204;—Clouston, T. S., Clinical lectures on mental diseases, 289;—Colbeck, E. H., Diseases of the heart, 290;—Collie, A., The infectivity of enteric fever, 123;—Constant, T. E., The naked-eye anatomy of the human teeth, 289;—Cross, M. I., and Cole, M. J., Modern microscopy, 203;—Davis, A. E., and Beaman, D., Eye, ear, nose, and throat nursing, 151;—Davis, E. P., A treatise on obstetrics, 292;—Draper, F. W., A text-book of legal medicine, 239;—Dudley, E. C., The principles and practice of gynecology, 387;—Dürck, H., Atlas and epitome of general pathologic histology, 151;—Edebohls, G. M., The surgical treatment of Bright's disease, 123;—Farabeuf et Varnier, Introduction à l'étude clinique et à la pratique des accouchements, 292;—Friedenwald, J., Diet in health and disease, 203;—Gould, G. M., Biographic clinics (vol. iii), 415;—Gowers, W. R. Lectures on diseases of the nervous system, 347;—Graetzner, E., Practical pediatrics, 204;—Griffith, F. R., A hand-book of surgery, 152;—Griffiths, L. M., Medical philology, 291;—Haab, O., Atlas and epitome of operative ophthalmology, 266;—Hall, G. S., Adolescence, 154;—Hall, W. S., A manual of experimental physiology, 121; A text-book of physiology, normal and pathological, 417;—Hare, H. A., A text-book of the practice of medicine, 290;—Hartmann, H., Travaux de Chirurgie, 312;—Holland, J. W., A text-book of medical chemistry and toxicology, 291;—Holmes, B., Appendicitis, 151;—Hughes, D. E., A compend of the practice of medicine, 266;—International clinics (vol. iv, 13 s.), 122; (vol. iii, 14 s.), 151; (vol. iv. 14 s.), 312; (vol. ii, 15 s.), 415;—International medical annual, 266;—Jackson, E., The ophthalmic year-book, 266;—James, S. P., First report of the anti-malarial operations at Mian-Mir, 152; On a parasite found in the white corpuscles of the blood of dogs, 265; Oriental or Delhi sore, 265;—Jelliffe, S. E., An introduction to pharmacognosy, 154;—Jennings, J. E., Color-vision and color-blindness, 414;—Keen, W. W., Addresses and other papers, 387;—Laumonier, J., New methods of treatment, 25;—Love, J. K., Diseases of the ear, 152;—Lydston, G. F., The surgical diseases of the genito-urinary tract, 311;—Marion, G., Chirurgie du système nerveux, 415;—May, C. H., Manual of the diseases of the eye, 414;—McFarland, J., A text-book of pathology, 151;—Medical and surgical report of the Bellevue and allied hospitals, 415;—Medical epitome series, Practice of medicine, 415;—Mettler, L. H., A treatise on diseases of the nervous system, 266;—Morris, H., Essentials of materia medica and prescription writing, 124;—Musser, J. H., Medical diagnosis, 25;—Nancrede, C. B., Essentials of anatomy, 26;—Nothnagel's Encyclopedia, Diseases of the blood, 414;—Paton, S., Psychiatry, 416;—Progressive medicine (vol. i), 292;—Publications of Cornell University Medical College, 265;—Pusey, W. A., The practical application of the Röntgen rays in therapeutics and diagnosis, 150;—Pyle, W. L., A manual of personal hygiene, 121;—Records of the Egyptian Government School of Medicine, 120;—Reed, B., Lectures to general practitioners on the diseases of the stomach and intestines, 25;—Reed, W., and others, Report on the origin and spread of typhoid fever in the U. S. Military Camps during the Spanish War of 1898, 348;—Reese, A. M., An introduction to vertebrate embryology, based on the study of the frog and chick, 151;—Ricketts, B. M., The surgery of the heart and lungs, 265;—Rolleston, H. D., Diseases of the liver, gall-bladder, and bile-ducts, 153;—Rose, A., Atonia gastrica (abdominal relaxation), 414;—Rosenbach, O., Physician versus bacteriologist, 121;—St. Clair, M. T., A compend of medical Latin, 26;—Senn, N., A nurse's guide for the operating room, 291;—Shaw, J. C., Essentials of nervous diseases and insanity, 26;—Smolensky, P., Traité d'hygiene procédés rapides de recherche des falsifications et altérations, 152;—Stoney, E. M. A., Bacteriology and surgical technic for nurses, 267;—Sutherland, W. G., Dispensing made easy. 415;—The pharmacopoeia of the United States, 388;—Transactions of the American Röntgen Ray Society, 349;—Tyson, J., A treatise on Bright's disease and diabetes, 202;—Walsham, H., The channels of infection in tuberculosis, 152;—Walton, J. R., Natural science in hygiene, 415;—Welch, W. M., and Schamberg, J. F., Acute contagious diseases, 292;—Wharton and Stille's Medical Jurisprudence, 289;—Woodruff, C. E., The effects of tropical light on white men, 267;—Wright, A. H., A text-book of obstetrics, 387.
Occlusion, partial, of blood-vessels, especially of the abdominal aorta, 346.
Osler, W., Letter to the graduates of the Johns Hopkins Medical School, 410.
Ovariotomy at extremes of life, survey of, 102.

Pancreatitis, acute, observations on several cases of, 355.
Paralysis, infantile, of the abdominal muscles, 11.
Parathyroid gland, tumor of, 87.
Pathology of fat and fatty degeneration, 1.
Pericarditis complicating acute lobar pneumonia, 334.
Pharmacology, contributions of to physiology, 351, 389.
Phlebitis, recurring, of obscure origin, 228.
Physiology, surgical, 269.
Platt, W. B., Fabricius Guilhelmus Hildanus, the father of German surgery, 7.
Pneumonia, lobar, action of the toxic agent of. Therapeutics, 321.
Pneumothorax, movability of the heart in, 300.
Pohlman, A. G., A note on the developmental relations of the kidney and ureter in human embryos, 49.
Pohlman, A. G., Abnormalities in the form of the kidney and ureter dependent on the development of the renal bud, 51.
Practical method of demonstration, 19.
Proceedings of the Johns Hopkins Hospital Historical Club, 412: Hurd, H. M., John Howard's observations on hospitals (1773-1790), 412; McCrae, T., History of typhoid fever, 413.
Proceedings of the Johns Hopkins Hospital Medical Society, 109, 146, 200, 237, 264, 288, 384, 411: Baer, W. S., Painful heels, 264;—Baetjer, F. H., Thoracic aneurisms, 387;—Barker, L. F., Bilateral exostoses on the inferior surface of the calcaneus, gonorrheal in origin (Pododynia gonorrhoica), 384; Bronzed diabetes, with enlargement of the liver and palpable spleen, 385; Perichondritis, probably of gonorrheal origin, 385;—Boggs, T. R., Bacteriological observations in some cases of bronchiectasis, 288;—Bunting, C. H., Congenital cystic kidney, 411;—Churchman, J. W., Atheromatous cyst of the scrotum, 264; Bladder calculus in an infant, 264; Congenital urethral stricture, 264; Traumatic atrophy of the testicle, 265;—Clark, J. G., The cure of uterine cancer, 149;—Clowes, G. H. A., The immunization of mice to cancer, 146;—Cole, R. I., Case of typhoid fever showing some unusual features, 118; Cystic kidney, 411; Experimental streptococcus arthritis, 114; Pulsating empyema, 411;—Crile, G. W., The scope and problems of surgical physiology, 201;—Cullen, T. S., Accessory omentum, 237; Adenocarcinoma of the umbilicus, 110; Cancer of the liver, 110; Fibroma of abdominal wall, 237; Primary carcinoma of the tubes, 237; Sarcomatous myoma, 237;—Cushing, H., Comparative surgery, 238;—Dawson, P. M., The blood pressure in different parts of the arterial tree, 202;—Dunham, T., Apparatus for the treatment of fracture of the femur, 147; Treatment of esophageal structure, 147;—Erlanger, J., Heart-block in mammals, 202; Fayerweather, R., Infectious arthritis, 412;—Ford, W. W., Hanging block cultivation of bacteria, 149; Thermophilic bacteria, 149; The ultraviolet rays, 149;—Halsted, W. S., Clinical features of thyroid hypertrophy, 288; Partial occlusion of the aorta, 202;—Howard, C. P., Gastric tetany, 148; Gastric ulcer: Clinical varieties and symptoms, 116;—Jones, H. C., The electric theory of matter, 237;—Kelly, H. A., Professor Smith on the Jersey mosquito, 115;—Kemp, G. T., Histology of the blood platelets, 200;—Lewis, H. W., Experiments on amphibian embryos, 238;—MacCallum, W. G., Demonstration of pathological specimens, 111; The pathology of tetany, 148;—McCrae, T., Gastric ulcer, Diagnosis and medical treatment, 116;—Osler, W., A case of arteriovenous aneurism, 146; Biliary cirrhosis of family type, 112; Report of a case of arteriovenous aneurism of the thigh, 119; Report of a case of ulcerative endocarditis, with embolism of the aorta, 118; Résumé of history of blood platelets, 200;—Pratt, J. H., Relation of blood platelets to disease, 200;—Sampson, J. A., Pathology of cervical cancer, 150;—Smith, H. L., Synesthesia, 149;—Thayer, W. S., Peripancreatic abscess, 148;—Thompson, W. L., Analysis of 221 cases of typhoid fever, 264;—Watts, S. H., Loss of entire lower lip, 109;—Williams, J. W., Inversion of uterus, 386.
Renal artery, first appearance of, and the relative development of the kidneys and Wolffian bodies in pig embryos, 60.
Renal decapsulation in nephritis, with report of a case,
Reuling, R., A case of right-sided infantile hemiplegia, with a description of the pathological changes found in the brain and the spinal cord, 21.
Robinson, G. C., The development of grave robbing in England, 42.
Sabin, F. R., On Flechsig's investigations on the brain, 45.
Sarcoma of the eye, involving chiefly the ciliary body, 402.
Slide-holding device, multiplex, 132.
Smith, H. L., Synesthesia, 258.
Situs transversus and atresia of the pylorus, 249.
Steiner, W. R., A contribution to the history of medicine in Maryland during the Revolution, 1775-1779, 241.
Stieren, E., A case of acquired cyst of the conjunctiva containing an embryonic tooth-like structure, 308.
Still to make absolute alcohol, 68.
Stokes, W. R., and Amick, A. L., Typhoid appendicitis without other intestinal lesions, 284.
Summaries or titles of papers by members of the Hospital or Medical School staff appearing elsewhere than in the Bulletin: 73:—Abbott, A. C., Address in State Medicine, before the Pennsylvania Medical Society, 73; Annual report of the Bureau of Health of Philadelphia for 1903, 73; Opening address, McGill Medical Faculty, 73;—Amberg, S., Primary malignant tumor of both adrenal glands in a child of two months, with secondary affection of the liver, 73;—Bardeen, C. R., and Baetjer, H., The inhibitive action of the Röntgen rays on regeneration in planarians, 73;—Barker, L. F., Is a trip to Europe worth its cost to the medical man? 73; Italy and the great antimalarial campaign, 73; Laboratory manual of anatomy, 73; Spain and Ramon y Cajol, 73;—Barker, L. F., and Abderhalden, E., Ueber aminosauren im Harn, 74;—Baumgarten, W., The methylene-blue eosin stains, 74;—Blumer, G., and Lartigau, A. J., Healed and quiescent pulmonary tuberculosis, 74;—Boggs, T. R., Ueber Beinflussung der Gerinnungszeit des Blutes im lebenden Organismus, 74;—Churchman, J. W., Christian science, 74; The determination of renal capability: Its present status, 74;—Cole, R. I., Experimenteller Beitrag zur Typhusimmunität, 74; The prevention of typhoid fever, 74; Ueber die Agglutination verschiedener Typhusstämme, 74;—Cook, H. W., The prevention of tuberculosis, 74;—Cullen, T. S., Tuberculous stricture of the ascending colon, with sudden total obstruction of the bowel, 74;—Cushing H., Intradural tumor of the cervical meninges, 74; Perineal zoster, with notes upon cutaneous segmentation postaxial to the lower limb, 74; Pneumatic tourniquets, with especial reference to their use in craniotomies, 74;—Dunton, W. R., A new slide box; also a method of recording embedded tissue, 74;—Elting, A. W., Congenital stenosis of the pylorus, with the report of a case successfully operated upon, 74; The pathology and treatment of tetanus, 74; Toxemia in association with tuberculosis of the cervical lymphatic glands, 74;—Flexner, S., and Noguchi, H., Upon the production and properties of anti-crotalus vein, 74;—Ford, W. W., The early diagnosis of cirrhosis of the liver, considered from the pathological standpoint, 74;—Ford, W. W., and Halsey, J. T., Contributions to the study of agglutinins and hemolysins, 74;—Gilchrist, T. C., Some additional cases of blastomycetic dermatitis, 74;—Gwyn, N. B., Carcinoma of abdominal cavity, etc., 74;—Halsted, W. S., The training of the surgeon, 74;—Hamburger, L. P., Creeping eruption: Its relation to myiasis, 74;—Hamman, L. V., The blood in acute leukemia, 74;—Hewlett, A. W., On the occurrence of lipase in the urine as a result of experimental pancreatic disease, 74;—Hirshberg, L. K., Simple class-room method for growing anærobic cultures, 74;—Hunner, G. L., Surgery of urinary tuberculosis in women, 74;—Hurd, H. M., Is nursing a profession? 74;—Jones, W., Ueber das Enzym der Thymus-

drüse, 74; Ueber die Selbstverdauung von Nucleoproteiden, 74; —Kelly, H. A., Rubber cushions for general surgical gynecological and obstetric use, 74;—Knox, J. H. M., The prophylaxis of summer diarrhea, 74; The Thomas Wilson Sanitarium for sick children, 74;—Ladd, L. W., The character of the Widal reaction in the present epidemic of typhoid fever, 74;—Loevenhart, A. S., Ueber die Gerinnung der Milch, 74;—Lynch, F. W., Kaiserschnitt und schwere Geburtsstörung infolge Ventro-fixation und Suspension, 74; Pathology of eclampsia, 74;—MacCallum, W. G., Diseases due to organic insufficiency, 74;—Marshall, H. T., Antitoxic serums in the treatment of disease, 75;—McCrae, T., Athritis deformans. The report of a series of one hundred and ten cases from the Johns Hopkins Hospital, 75; The treatment of typhoid fever in the Johns Hopkins Hospital, 75;—Nuttall, G. H. F., Canine piroplasmosis, 75; Directions for preserving filariæ, 75;—Nuttall, G. H. F., and Inchley, O., An improved method of measuring the amount of precipitum in connection with tests with precipitating antisera, 75;—Nutting, M. A., A school for social workers, 75; State reciprocity, 75; The Tuberculosis Exposition, Baltimore, 75; Visiting nurses in the homes of tuberculous patients, 75;—Opie, E. L., An experimental study of the relation of cells with eosinophile granulation to infection with an animal parasite (Trichina spiralis), 75; Lesions peculiar to the pancreas and their clinical aspect, 75; The occurrence of cells with eosinophile granulation and their relation to nutrition, 75; The relation of cells with eosinophile granulation to bacterial infection, 75; Zonal necrosis of the liver, 75;—Osler, W., Chronic cyanotic polycythemia with enlarged spleen, 75; On the surgical importance of the visceral crises in the erythema group of skin diseases, 75; On the visceral manifestations of the erythema group of skin diseases, 75; —Perkins, R. G., Trypanosomiasis, 75;—Pleasants, J. H., The increasing mortality from pneumonia in Baltimore, and its causes, 75;—Robb, H., Acute dilatation of the stomach complicating an abdominal section, 75; Conservatism in pelvic surgery, 75; The early diagnosis of cancer of the fundus, with report of cases, 75; The streptococcus in gynecological surgery, 75;—Rosenheim, S., and Warfield, M., A case of fibroadenoma of the trachea, with remarks on tumor of the trachea in general, 75;—Schenck, B. R., The newer methods of detecting renal insufficiency. Cryoscopy and the phlorizin test, 75;—Spratt, C. N., An improved snare for the removal of the faucial tonsil, 75; The removal of septal spurs and the correction of deviations of the septum by more rational methods, 75;—Steiner, W. R., A case of typhoid fever presenting an arterial complication, probably an arteritis, 75; The Reverend Gershom Bulkeley, of Connecticut, an eminent clerical physician, 75;—Thayer, W. S., On the late effects of typhoid fever on the heart and vessels, 75;—Theobald, S., Are tenotomies for hyperphoria necessarily more uncertain in their results than those for esophoria and exophoria? 75;—Warfield, L. M., Grave anemia due to hookworm infection, 75; Observations on uncinariasis, 75; Summer diarrhea of infants, 75;—Woolley, P. G., Some pulmonary lesions produced by the bacillus of hemorrhagic septicemia of carabaos, 75; Frambesia: Its occurrence in natives of the Philippine Islands, 75;—Woolley, P. G., and Jobling, J. W., A report on hemorrhagic septicemia in animals in the Philippine Islands, 75.

Surgery, comparative, 179.

Surgery, neurological, special field of, 77.

Surgery of the posterior mediastinum; its past and its future, 125.

Surgical physiology, 269.

Synesthesia, 258.

Teaching of anatomy as illustrated by Professor Barker's Manual, 29.

Testing the ocular muscle balance for near, as well as for distant vision, importance of, 10.

Thayer, W. S., Cotton Mather's rules of health, 293; Observations on several cases of acute pancreatitis, 355.

Theobald, S., The importance of testing the ocular muscle balance for near, as well as for distant vision, 10.

Tissues, fixation of, by injection into the arteries, 66.

Tuberculin in orthopedic surgery, diagnostic value of, 13.

Tumor of the parathyroid gland, 87.

Typhoid appendicitis without other intestinal lesions, 284.

Urethral stricture, congenital, associated with hematuria and symptoms suggesting renal disease, 256.

Vaginal cysts, 207.

Wiel, H. I., A survey of ovariotomy at extremes of life. Report of a case in a girl aged 5, 102.

Wiesenthal's (Dr. Charles Frederick) medical reports, 407.

Winne, C. K., A report upon the agglutination reactions of the Bacillus dysenteriæ (Shiga) with the blood serum of patients suffering with summer diarrhea, 93.

Woolley, P. G., A case of sarcoma of the eye, involving chiefly the ciliary body, 402; Bacillus violaceus Manilæ, 89.

Young, H. H., The early diagnosis and radical cure of carcinoma of the prostate, 315.

ILLUSTRATIONS.

Infantile paralysis of the abdominal muscles (Plate I, Figs. 1-3), 12.

Diagram of thorax, abdomen and pelvis, 19.

Right-sided infantile hemiplegia (Plates I and II, Figs. 1-9), 22.

Anatomical laboratory of the University of California (Fig. 1), 34; (Fig. 4), 35; (Figs. 9 and 11), 36; (Plates III-VI, Figs. 2-3, 5-10, 12), 36.

Sections of brain (Plate VII, Figs. 1-4), 48.

Abnormalities in the form of the kidney and ureter, 53, 56 and 59.

Diagram showing relative size of the kidney and Wolffian body, 63.

Relative development of kidneys and Wolffian bodies (Plates VIII-IX, Figs. 1-7), 64.

Outline of brachial artery and its branches (Fig. 1), 65.

Improved injection apparatus (Fig. 1), 66.

Still for making absolute alcohol (Figs. 1-5), 69.

Right lung showing aneurism, 100.

Gross appearance of longitudinal section of tumefied ovary with adherent tube, 108.

Multiplex slide-holding device, 132.

Hyperplasia of the chromophile cells of the hypophysis as the cause of acromegaly (Plates X-XI), 164.

Photographs of William Harvey and Michael Servetus, 166.

Figures showing ligated vessels of the arm (Figs. 1-2), 172.

Hemorrhagic cyst of thyroid gland (Figs. 1-6), 180-183.

Utero-vaginal prolapse (Fig. 7), 185.

Canine neoplasm (Figs. 8-31), 186-195.

Hernia in dogs (Figs. 32-33), 196-197.

Vaginal cysts (Figs. 1-21), 208-216.

Force of contraction of the gall-bladder (Plates XII-XIII, Figs. 1-7), 236.

Situs transversus and atresia of the pylorus (Figs. 1-3), 252-253.

Needle and clamp for injecting lymphatics (Figs. 1-4), 274.

Marcello Malpighi (Plate XIV), 275.

Typhoid appendicitis without other intestinal lesions (Plate XV, Figs. 1-4), 286.

Movability of the heart in pneumothorax (Figs. 1-3), 301-302.

Acquired cyst of the conjunctiva containing an embryonic tooth-like structure, 309.

Carcinoma of the prostate (Plates XVI-XVII, Figs. 1-8), 320.

Unusually large aortic aneurysm (Plate XVIII, Figs. 1-4), 332.

Figures showing position of palpable mass or tumor in cases of pancreatitis, 356-360.

Diaphragmatic grooves on the liver, 369, 373 (Plate XIX, Figs. 1-6), 376.

Cardiograms obtained from a case of operative defect in the chest wall, (Plate XX, Figs. 1-4), 397.
Fibroma of abdominal wall (Fig. 1), 398; Primary carcinoma of the right Fallopian tube (Fig. 2), 399; Accessory and twisted omentum (Fig. 3), 400.

ERRATUM.

In Dr. John W. Dewis's letter, on page 199 of the BULLETIN, the signature should have been John W. Dewis, instead of John W. Lewis, as printed.

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